

PCTWORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

BA

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : G06K 9/00	A1	(11) International Publication Number: WO 99/42949
		(43) International Publication Date: 26 August 1999 (26.08.99)

(21) International Application Number: PCT/US99/03282

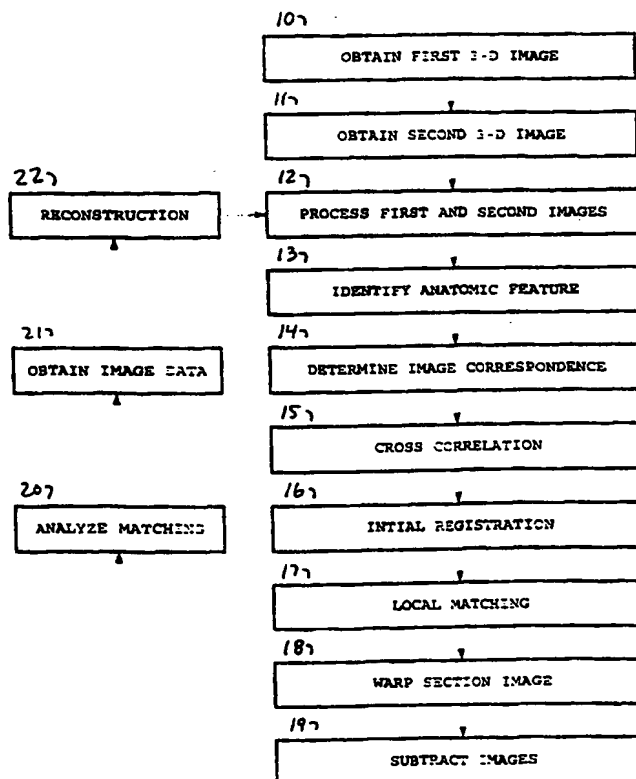
(22) International Filing Date: 22 February 1999 (22.02.99)

(30) Priority Data:
09/027,468 23 February 1998 (23.02.98) US(71) Applicant: ARCH DEVELOPMENT CORPORATION
[US/US]; Room 405, 5640 South Ellis Avenue, Chicago,
IL 60637 (US).(72) Inventors: XU, Xin-Wei; 1042 Park Crest Drive, Darien, IL
60561 (US). DOI, Kunio; 6415 Lane Court, Willowbrook,
IL 60521 (US).(74) Agents: KUESTERS, Eckhard, H. et al.; Oblon, Spivak,
McClelland, Maier & Neustadt, P.C., Suite 400, 1755
Jefferson Davis Highway, Arlington, VA 22202 (US).(81) Designated States: AU, CA, JP, European patent (AT, BE,
CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC,
NL, PT, SE).**Published**
With international search report.

(54) Title: METHOD AND SYSTEM FOR THE AUTOMATED TEMPORAL SUBTRACTION OF MEDICAL IMAGES

(57) Abstract

Method and system for detection of interval change in medical images. Three-dimensional images, such as previous and current section images (10 and 11) in CT scans, are obtained. An anatomic feature, such as lungs, is used to select sections containing lung by a gray-level thresholding technique (13). The section correspondence between the current and previous scans is determined automatically. The initial registration of the corresponding sections in the two scans is achieved by a rotation correction (14) and a cross-correlation (15) technique. A more accurate registration between the corresponding current and previous section images is achieved by local matching (17). A nonlinear warping process (18) which is also based on the cross-correlation technique is applied to the previous image to yield a warped image after the matching. The final subtracted section images (19) were derived by subtracting of the previous section images from the corresponding current section images. Interval changes such as a change in tumor size and a newly developed pleural effusion are enhanced significantly.



FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

Method and System for the Automated Temporal Subtraction of Medical Images

CROSS-REFERENCE TO RELATED APPLICATIONS

The present is related to automated techniques for automated detection of abnormalities in digital images, for example as disclosed in one or more of U.S. Patents 4,839,807; 4,841,555; 4,851,984; 4,875,165; 4,907,156; 4,918,534; 5,072,384; 5,133,020; 5,150,292; 5,224,177; 5,289,374; 5,319,549; 5,343,390; 5,359,513; 5,452,367; 5,463,548; 5,491,627; 5,537,485; 5,598,481; 5,622,171; 5,638,458; 5,657,362; 5,666,434; 5,673,332; 5,668,888; as well as U.S. applications 08/158,388; 08,173,935; 08/220,917; 08/398,307; 5,790,690; 08/523,210; 08/536,149; 08/536,450; 5,832,103; 5,732,697; 08/562,087; 08/757,611; 08/758,438; 08/900,188; 08/900,189; 08/900,191; 08/900,192; 08/900,361; 08/900,362; 08/979,623; 08/979,639; 08/982,282; 09/028,518 and 09/027,685 each of which are incorporated herein by reference in their entirety. Of these patents and applications, 5,319,549 and 08/900,362 are of particular interest.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH

The present invention was made in part with U.S. Government support under grant numbers CA 62625 and CA 64370 (National Institutes of Health) and DAMD 71-96-6228 (U.S. Army). The U.S. Government has certain rights in the invention.

BACKGROUND OF THE INVENTION

Field of the Invention

The present invention is related to temporal analysis of medical images and, in particular, to the analysis of computed tomographic images using automated temporal subtraction.

Discussion of the Background

The application of a temporal subtraction technique to radiographic images such as chest images can significantly enhance some subtle interval changes existing in sequentially obtained images which might be missed by radiologists. These interval changes may be very important in enabling radiologists to detect some diseases, such as early lung cancer, or to assess the effects of treatment on known lesions. Difazio et al., in Digital chest radiography:

Effect of temporal subtraction images on detection accuracy, Radiology, 202:447-452 (1997) reported that the use of the temporal subtraction technique for sequential chest images can significantly increase radiologists' diagnostic accuracy in identifying interval changes.

When radiologists interpret a thoracic computed tomography (CT) scan of a patient, they commonly view it side by side with the most recent previous scan of the same patient. Such comparison readings also help radiologists to identify interval changes or to assess the effects of treatment on known lesions between two consecutive thoracic CT examinations. However, it is difficult and time-consuming for radiologists to compare current and previous (temporally sequential) thoracic CT scans to identify new findings or to assess the effects of treatments on known lesions, because this requires a systematic visual search and correlation of a large number of images (sections) in both current and previous scans. Generally, more than 25 section images were reconstructed from a thoracic CT scan with a section thickness of 10 mm. The number of section images may be much higher when a high-resolution scan (section thickness of 3 mm) is required.

Viewing several images can be difficult because of variations in the images. For example, the positioning of the patient may be different at the various times the images are produced. Patient breathing and cardiac pulsation can also produce variances in the images. It is important to be able to register images to detect interval changes where corresponding features in the images can be subtracted from each other.

The techniques for temporal subtraction, such as described in U.S. Patent 5,319,549, have only been applied to two-dimensional imaging. These techniques register and subtract two-dimensional images, such as chest radiographs.

SUMMARY OF THE INVENTION

It is an object of the present invention to provide improved automated temporal subtraction of images.

A second object of the invention is to enhance interval changes in images.

A further object of the present invention to perform automated temporal subtraction for three-dimensional scanning.

Another object of the present invention is to perform automated temporal subtraction using matching images in the direction of scanning.

A still further objection of the invention is to three-dimensionally match two images and two-dimensionally match corresponding sections of the two images.

These and other objects of the invention are achieved by a method, system and computer program product for detecting interval change in images. In the method according to the invention, first and second three-dimensional images of a subject are obtained. The first and second images are typically current and previous images of a subject. The first and second images are matched. The first image is non-linearly warped to produce a warped image and the warped image is subtracted from the second image. The subtraction can produce and/or enhance interval changes in the first and second images.

A portion of the first image may be selected using an anatomic feature in the first image. A portion of the second image may be selected using the same anatomic feature. Relative areas of the anatomic feature in the first and second images may be determined. The portions of the first and second images may be selected using the relative areas determined in the first and second images, respectively.

Determining the relative areas may be done by thresholding the first and second images to obtain corresponding regions in the first and second images. An area of each of these regions is determined and the relative areas are then determined as a ratio of an area of these regions to remaining areas in the images.

The matching of the images may be done by comparing the first and second relative areas. The matching may also be done by determining a first relationship of the area of the anatomic feature in the first and second images. Averages of the relationships of the areas can then be determined and sections of the first and second images corresponding to the averages can be selected.

It is also possible to select one section in the first image and a number of sections adjacent to that section. These sections are compared to one section selected in the second image. One of the sections selected in the first image is then matched to the section in the second image. Remaining sections in the first image may then be matched in a one-to-one manner to remaining sections and the second image.

Cross-correlation may be used in matching the images. The matching may also consist of initially matching the first image to the second image and then locally matching the first image to the second image. The initial matching may consist of determining whether the

first image is rotated and correcting the rotation, and determining vertical and horizontal shifts of the first image relative to the second image. Cross-correlation may use the vertical and horizontal shifts in matching the first and second images.

The local matching may consist of selecting regions of interest in the first and second images and determining horizontal and vertical shifts of regions of interest in the first image relative to regions of interest in the second image. The horizontal and vertical shifts may then be curve-fitted and the used in a warping process to warp the first image. The warped image may be subtracted from the second image to produce a subtracted image.

The method may also include analyzing the registration of the subtracted images. If the registration is inadequate, the image data may be retrieved and the current image may be reconstructed at a different reconstruction starting point. The analysis of the registration may be performed using histogram analysis.

The method may be advantageously applied to computed tomography (CT) scanning. In this case, the three-dimensional matching consists of matching the current and previous scans while the two-dimensional matching consists of matching the corresponding sections of the current and previous CT scans.

The invention may also be implemented in the form of a computer program product comprising a computer storage medium and a computer program code mechanism embedded in the computer storage medium. Code devices are then configured to implement various steps in detecting interval change.

These objects are also achieved by an interval change detecting system having at least one of a three-dimensional image storage device and a three-dimensional image acquisition device. A scanning direction image matching device is connected to one of the acquisition device and storage device. The system may also include a two-dimensional image matching device and a relative area determination circuit. Invention may further include a local matching circuit, a warping circuit and a cross correlation circuit. It is also possible that the system contains a registration analysis circuit which may consist of a histogram analysis circuit, an image data retrieval circuit and an image data reconstruction circuit.

BRIEF DESCRIPTION OF THE DRAWINGS

A more complete appreciation of the invention and many of the attendant advantages

thereof will be readily obtained as the same becomes better understood by reference to the following detailed description when considered in connection with the accompanying drawings, wherein:

FIG. 1 is a diagram of an embodiment of the method according to the invention;

FIGS. 2A and 2B are section images of a current thoracic CT examination by helical scanning and section images of a previous thoracic CT examination of the same patient, respectively;

FIG. 3 is a graph of the relative lung area versus section number for the CT scans shown in FIGS. 2A and 2B;

FIG. 4A is an example of a segmented, low-resolution image from the mid-section image of a current CT scan and FIGS. 4B-4F are examples of ROI images obtained from the previous scan around the mid-section, respectively;

FIG. 5A is an image illustrating the definition of the orientation of the lungs;

FIG. 5B is the image of FIG. 5A before rotation correction for lung orientation;

FIG. 5C is the image of FIG. 5A after rotation correction for lung orientation;

FIG. 6A is a section image from a current scan;

FIG. 6B is a corresponding ROI section image from a previous scan;

FIG. 6C is a diagram illustrating the definition of horizontal and vertical shifts (Δx and Δy) of the image of FIG. 6B relative to the image of FIG. 6A;

FIGS. 7A and 7B are diagrams illustrating the distribution of template ROIs on a previous section image and the distribution of search area ROIs on a current section image, respectively;

FIG. 8A is a diagram illustrating horizontal shifts (Δx) of all pairs of templates relative to the search area ROIs;

FIG. 8B is a diagram of a two-dimensional third-order polynomial fit of the horizontal shifts;

FIG. 9A is a diagram illustrating vertical shifts (Δy) of all pairs of templates relative to search area ROIs;

FIG. 9B is a diagram of a two-dimensional third-order polynomial fit of the vertical shifts;

FIG. 10A is an original section image from a previous scan;

FIG. 10B is the section image of FIG. 10A after nonlinear warping;
FIG. 11A is a diagram of section images of a current scan;
FIG. 11B is a diagram of section images of a previous scan;
FIG. 11C is a diagram of the subtracted section images obtained using the images of FIGS. 11A and 11B;
FIG. 12A is a diagram of section images of a current scan;
FIG. 12B is a diagram of section images of a previous scan;
FIG. 12C is a diagram of the subtracted section images obtained using the images of FIGS. 12A and 12B;
FIG. 13 is a diagram of the system according to the invention; and
FIG. 14 is a diagram of the image processing device according to the invention.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

With reference to the drawings, particularly FIG. 1, a first embodiment of the method according to the invention will be described. First (step 10) and second (step 11) three-dimensional images of a patient are obtained. The first and second images typically correspond to current and previous images of the same subject. The first and second images may also be two previous images of the same subject, where interval changes between the two images are desired. As an example of the invention, thoracic helical computed tomography (CT) scans of patients are obtained from a CT scanner, such as a GE HiSpeed CT/i. In CT scanning the first and second images are commonly referred to as current and previous scan. The scans are reconstructed from the image data acquired by the scanner. However, the invention is not limited to CT images. Other types of three-dimensional images, such as MRI images, may be used. The scanning pitch and section thickness for generating the CT images were 1 and 10 mm, respectively. Other values for these parameters may also be selected.

The images may be obtained directly from a scanner or may be obtained from a storage device. Typically the previous section images are from an earlier scan and have been stored. It is also not required that the images are obtained on the same or the same type of scanner. Further, the method according to the invention can also use the acquisition data (step 21) of the scans and then reconstruct the images (step 22) before further processing,

which is also described in more detail below.

In this example, the reconstructed digital section images (with DICOM header) was used. The matrix size of each reconstructed section image was 512×512 pixels. The pixel size of the section images can vary because of the different field of view (FOV) used for reconstruction in the clinical environment. The FOV for the reconstruction used in a clinical environment can vary from 29 to 42 cm. The maximum FOV allowed for reconstruction is 48 cm for the GE scanners used. In this case (including the current and previous scans), a correction factor should be applied for the FOV to all of the section images to ensure a uniform pixel size for every section image. The gray scale of the section images was 12 bits (pixel values from 0 to 4095), which corresponds to Hounsfield units (HU) of -1023 to 3072. Notice that air, water, and bone correspond to HU of -1000, 0, and 1000, respectively. In consideration of computer storage and CPU time, it is sometimes desirable to reduce the matrix size and gray scale of the thoracic CT section images to, for example, 256×256 pixels and 10 bits, respectively.

A scan for a thoracic CT examination can include a large number of section images (each with 10 mm thickness, in this example) which extend from approximately the neck of the patient down to the lower abdomen, as shown in FIGS. 2A and 2B. An interval change is usually detected by comparing anatomic features in the previous and current scans. To demonstrate the invention, the lungs were chosen as the anatomic feature in the images to be compared. However, the method is applicable to other features in the image, particularly solid organs such as the liver and kidney, or to bone and enhanced vessels.

Two pre-processing steps, i.e., segmentation of the anatomic feature and Gaussian filtering, are applied in step 12 to the first and second images. In the example, the lungs are segmented from selected sections from both the current and previous scans. The lung segmentation was achieved by use of a gray-level thresholding technique. The CT images are digital gray-scale images having a plurality of pixels (i.e., 512×512). The gray levels of the lungs corresponded generally to HU of -900 to -400. With the gray-level thresholding technique, pixels with HU above -400 and below -900 were eliminated to provide the lung area. The lung area may be approximated by a rectangle. The rectangle may be determined using horizontal and vertical profiling to detect the upper, lower and side lung edges based upon changes in pixel values. A 9×9 smooth Gaussian filter was employed to blur the vessel

structures inside the lungs.

In step 13 the portions of the images that contain the anatomic feature are identified. The portions of the images corresponding to the anatomic feature of interest, the lungs in this example, will be referred to as lung sections. For the CT images shown in FIGS. 2A and 2B, the lung sections are from section #5 to #24 and section #4 to #24, respectively. To select the lung sections from a thoracic scan, a parameter for each section in the scan is calculated, namely, the relative lung area. Here, relative lung area was defined by the ratio of the number of pixels in the section image with HU from approximately -900 to -400 to the number of remaining pixels in that section image. As mentioned above, the pixels with HU from approximately -900 to -400 mainly correspond to lung structures in the thoracic CT scan.

As mentioned above, other features such as the liver, kidney, bone or enhanced vessels may be chosen. The vessels are enhanced by injecting contrast media into the bloodstream. The image is thresholded to separate pixels corresponding to the liver or kidney, or to bone or enhanced vessel. Since these organs and features may be relatively small, it is preferable that higher resolution scanning is used with a thinner slice.

FIG. 3 shows the relative lung area plotted for each section for the two CT scans in FIGS. 2A and 2B. Obviously, the value of the relative lung area was very small (close to zero) for sections in the abdomen and neck areas. Lung sections are selected from the scan that have a certain relative lung area. In this example, a lung section was selected from the scan if the relative lung area was larger than 0.1. Other ratios may be chosen.

Once the portions of the images that contain the anatomic feature are identified, the correspondence between the first and second images is determined (step 14). The selected lung section images from both the current and previous thoracic CT scans are used to determine the section correspondence between the two scans. First the curves of relative lung area (see FIG. 3) of the two scans are generated and compared to determine, approximately, the shift in the scanning direction (i.e., in the z-axis) between the two scans (step 15). The average section number of each curve was then calculated by summation of each weighted section number with its corresponding value of the relative lung area. The average section numbers are 14.7 and 13.7 for the curves of relative lung area of the current and previous scans in FIG. 3, respectively. The difference in the average section number between the two scans is related to the starting positions in the two consecutive scans. Therefore, the

difference between the two average section numbers indicated the overall shifts in the scanning direction (i.e., in the z-axis) between the two scans. Intuitively, for the same patient, if the table position and the patient scanning starting position were kept the same in the two consecutive scans, then the two curves of the relative lung area should match exactly, and the two average section numbers should be the same. However, it is very difficult to keep these positions unchanged in a clinical environment.

In the two images a point is selected as an initial benchmark for finding the correspondence between the two images. For the thoracic CT scan example, the section image whose section number equals the nearest integer of its average section number is defined as the mid-section image of the scan. The mid-sections of the current and previous scans were used as the initial benchmark. The mid-section and several adjacent sections (two above and two below, a total of five sections, for example) are selected from the previous scan for comparison, one by one, with the mid-section from the current scan to find a pair of the best-matched section images in the two scans at the region around the mid-lung. For this comparison, the matching of the overall lung shape is more important than the detailed structures, such as vessels in the lungs.

A cross-correlation technique is used (step 15) to compare the mid-section image of the current scan to each of the selected (five) section images of the previous scan. To apply the cross-correlation technique, region-of-interest (ROI) images selected from the five section images of the previous scan are used instead of the section images themselves. Each ROI image has a width and height large enough to encompass the lungs for each section. In this example, the width and height of the ROI are 200 and 126 pixels, respectively. The center of the ROI for a section image is selected as the center of the lung area of that section image. FIG. 4A is an example of a section image while FIGS. 4B-4F are examples of the ROI section images selected for this comparison.

The normalized cross-correlation values between the mid-section of the current scan and each of the five ROIs of the previous scan were then calculated. The pair of sections which provided the highest cross-correlation value was identified as the corresponding section pair between the current and previous scans. The remaining sections in both scans were then correlated rigidly based on the determined corresponding pair with the highest cross-correlation value, i.e., in a one-to-one manner. Any remaining unpaired sections are

ignored for further processing.

In a three-dimensional scan, such as a CT scan, a number of sections or slices are reconstructed. These slices is generally treated as having x-axis and y-axis data, while the scanning is preformed in the z-axis direction. Thus, the present invention matches corresponding sections or slices in the previous and current images two-dimensionally, in the x- and y-axis directions, and matches the scans (containing a number of section or slices) three-dimensionally in the z-axis direction.

After the establishment of the one-to-one section correspondence in the current and previous images, i.e. matching in the scanning direction (three-dimensional matching), the initial registration of the paired section images is performed in step 16 (two-dimensional matching). For the CT sections, each pair of corresponding section images in the two scans are initially registered. The initial registration of the corresponding section images in the two scans included two steps: a rotation correction and the determination of vertical and horizontal shifts of the previous section image relative to the current section image. The lungs in the thoracic CT section images were often oriented toward the right or left side because of patient movement, breathing, and lying on the back improperly during the scanning. FIG. 5A illustrates a section image with the lungs oriented to the left side. Commonly, the lung orientation is only slightly different for different sections in a given scan. However, the difference in lung orientations could be very large for sections from different scans.

The lung orientation is defined by the angle (α) between the vertical axis (Y axis) of the section image and the normal line (N) to the line segment (L) which goes through the lowest points in each lung, as illustrated in FIG. 5A. The orientation of each section image in both the current and previous scans was determined and corrected using known techniques. FIGS. 5B and 5C show an example of before and after the rotation correction for the orientation of the section image of FIG. 5A.

The relative shifts in the vertical and horizontal directions between the previous section image and the corresponding current section image were determined also by use of the cross-correlation technique with the segmented, low-resolution images, as shown in FIG. 6. The similar ROI image (200×126 pixels, including the entire lungs) from the previous section image was again used for this purpose. The ROI image was moved through the current

section image pixel by pixel, and the normalized cross-correlation value at each pixel was obtained. The horizontal and vertical shifts (Δx and Δy) of the previous section image relative to the current section image were determined when the cross-correlation value reached its maximum value, as shown in FIG. 6B.

After the process of initial registration, local matching is applied to the images to obtain more accurate registration (step 17). For the CT scans, the corresponding pair of sections of the current and previous scans are locally matched. The local matching technique is again based on the cross-correlation technique, which results in nonlinear warping of the previous section image. To perform the local matching, many small ROIs were selected automatically over the lung area of the section image, as shown in FIGS. 7A and 7B. Recall that the lung area in the section image was approximated by a rectangle. An ROI selected in the previous section image is called a template ROI (or simply a template), and that selected in the current section image is called the search area ROI. The sizes of the template and search area ROIs were 16×16 and 32×32 pixels, respectively. Other sizes may be used. The distance between the centers of the two adjacent ROIs was fixed as 16 pixels for both the template and search area ROIs. For each pair of template and search area ROIs, the template was moved through the search area ROI pixel by pixel. The normalized cross-correlation value at each pixel was calculated. The maximum value of the cross-correlation indicated that the subregion in the search area ROI where the template overlapped was the "best" match with the template. The assignment of the template and search ROIs could be reversed, i.e., the search ROI could be selected in the previous section image.

The horizontal and vertical shifts (Δx and Δy) between the center of the template and the center of the search area ROI for the best match was thus determined. FIGS. 8A and 9A indicate the distributions of the shift values Δx and Δy , respectively, derived for all pairs of template and search area ROIs in FIGS. 7A and 7B. It should be noted that the local matching should be limited to the area of the anatomic feature in the images (i.e., the lung area in the section images).

A two-dimensional curve fitting with third-order polynomials, based on a least-squares method, was used for fitting Δx and Δy in order to obtain the continued shift values at each pixel for the purpose of nonlinear warping of the previous section image. Other curve fitting techniques may also be used. FIGS. 8B and 9B illustrate the fitted shift

values of Δx and Δy , respectively, at every pixel of the previous section image within the lung area, as shown in FIGS. 7A and 7B.

To obtain the subtracted section image between the current and previous sections, the previous section image was warped (step 18) and then subtracted (step 19) from the current section image. The warping of the previous section image is based on the fitted shift values, as described in detail U.S. 5,319,549, application Serial No. 08/900,362, and Kano et al., *Digital image subtraction of temporally sequential chest images for detection of interval change*, Med Phys, vol. 2, No. 1 pp. 453-461 (1994). FIGS. 10A and 10B illustrate a previous section image and its warped image.

EXAMPLE

A total of 14 cases (14 pairs of temporally sequential thoracic CT scans) were used to demonstrate the method according to the invention. The time interval between the current and previous thoracic CT scans was varied from two to seven months. The truth of the presence or absence of interval changes was obtained by an experienced radiologist reading the images. Two cases were reported to have interval changes, and the other cases had no interval changes, according to the radiologists.

FIGS. 11A-11C show the case in which an anterior mediastinal mass (at the left side in the section images) increased in size from 3 cm in the previous scan to 4 cm in the current scan. On the subtracted section images (FIG. 11C), the dark area surrounding the mass indicates that the mass is increased in size. The dark area is indicated by the arrows. With the method according to the invention, the new findings or interval changes in the current sections are shown as dark patterns on the subtracted section images. Also, for this case, the right hilar region had increased in size in the current section images; this was again shown as a dark region in the subtracted section images, as also seen in FIG. 11C.

FIGS. 12A-12C show another case of temporal subtraction, in which a new pleural effusion (indicated by the arrows in FIG. 12C) developed at the lung bases in the current section images. The newly developed pleural effusion may be due to metastatic disease or to another cause. On the subtracted section images (FIG. 12C), the dark structures with a waning moon shape in the left and right lower parts of the lungs illustrate the newly developed symptom.

It will be noted that some vascular structures remained in the subtracted section

images. The main reason for misregistration of these vascular structures in the current and previous sections was probably the partial volume effect due to the variation in the depth of patient inspiration during the scan, and also to the different starting positions for the scans in the two sequential CT examinations. Although it is difficult to control patient breathing in different scans, it is possible to overcome the partial volume effect caused by the different starting positions in two sequential scans, if the raw data from the helical scanning are available.

In a modification of the method according to the invention, the raw scanning data are obtained (step 19) and the section images of a helical scan can be reconstructed for different starting locations on the z-axis from the data (step 20). In the clinical situation, the reconstruction usually starts at the position where the scanning starts physically. The registration of the corresponding sections in two scans can be greatly improved if the reconstruction starting position of one scan can be properly adjusted within the range of one section thickness (i.e., 10 mm in this example), with an accuracy on the order of 1 mm. Whether to use the raw data to reconstruct the images may be determined using histogram analysis and subtracted image to determine the degree of misregistration. The histogram has a broader distribution when there is misregistration since there are more light and dark patterns in the subtracted image. On the other hand, the histogram has a narrower distribution when there are fewer light and dark patterns. A measure of the breadth or narrowness of the histogram may be used to automatically determine if the registration is acceptable.

If the histogram analysis shows that there is significant misregistration, the current image may be reconstructed using a different starting point. The new starting point can be determined iteratively by shifting the previous starting point by a fixed distance, such as 1 mm. The scanner has the capability of image reconstructing based on a number of input parameters, including starting a reconstruction at any point with a section. The input parameters may be adjusted to produce a better match of the current and previous images. The method according to the invention is repeated with the newly reconstructed images. When the registration is found to be acceptable using the histogram analysis, the images can be output.

FIG. 13 is a diagram of the system according to the invention. Images (or data) is obtained from image acquisition device 100 and image storage device 101. Image

acquisition device 100 may be a CT scanner or an MRI scanner, for example. Image storage device 101 may be a memory device, an optical disk reader, when the images or data are stored on optical disk, or the PACS system (picture archiving communication system) where the images are usually stored on magnetic tape. An image transfer device 102 transfers images from devices 100 and 101 to image processing device 103. Device 103 carries out the operations described above in connection with the method embodiment. For example, device 103 processes the image by conducting the thresholding operation on the images and the Gaussian filtering. Device 103 also performs the relative area determinations, matching and cross-correlations, as well as the warping and subtracting. Device 103 may contain memory to store data or images on which the operations are being carried out, or intermediate results.

Devices 100-103 are controlled by a controller 104. Controller 104 may be, for example, a computer. Controller 104 also controls the output or display of the results of device 103 sent to output device 105. Output device 105 may be a video display terminal or a printer. A data entry device 106, such as a keyboard and pointing device, is provided to enter commands for the controller 104 to control the various devices to carry out the operations on the images or image data.

The system according to the invention may also be implemented in software run on a computer. Software code devices maybe written to carry out the various operations on the images. Thus, the invention may also be implemented as a program embedded in a computer-readable storage medium, such as a magnetic or optical disk.

FIG. 14 is a more detailed diagram of device 103. Device 103 includes an image processing circuit 110 that performs thresholding and, if needed, filtering operations or other desired image processing. The image after processing by circuit 110 used by circuit 111 to determine the relative area of an anatomic feature, such as the lungs. Image matching circuit 112 performs the cross-correlation to determine the initial registration of the two images, and ROI selection in the images for this operation. In the CT example, the mid-section image from the current is compared with the five selected section images from the previous scan using the cross-correlation operation to match the two scans.

Image registration circuit 113 performs the rotation correction and the determination of the vertical and horizontal shifts, using the matched images.

Local matching circuit 114 locally matches the images (the section pairs in the CT

example) for accurate registration. Template and search ROIs are selected and the distribution of the horizontal and vertical shifts are determined using cross-correlation.

A curve-fitting circuit 115 fits the distribution of the horizontal and vertical shifts using a polynomial fit, as discussed above. The fitted distribution is used by warping circuit 116 to produce the warped image, which is subtracted by subtraction circuit 117 from the current image to produce the subtracted images.

The circuit may also contain a registration analysis circuit 118 that determines if the registration is acceptable. If the registration is not found to be acceptable, using histogram analysis, for example, the circuit causes the system to obtain the image data (CT scanning data in this example) and the data is used by the image acquisition device to reconstruct the section images at a more desired starting point to eliminate image artifacts such as the partial volume artifact. This operation may be done iteratively.

The automated registration and subtraction method and system according to the invention, particularly when applied to temporally sequential section images, can enhance some interval changes effectively, such as changes in tumor size and the development of new nodules and pleural effusions. Therefore, the method and system according to the invention may help radiologists to identify and assess subtle interval changes in thoracic CT examinations more quickly and accurately.

Obviously, numerous modifications and variations of the present invention are possible in light of the above teachings. It is therefore to be understood that within the scope of the appended claims, the invention may be practiced otherwise than as specifically described herein.

Claims:

1. A method for detecting interval change, comprising:
obtaining a first three-dimensional image of a subject;
obtaining a second three-dimensional image of said subject;
matching said first and second images;
nonlinearly warping said first image to produce a warped image; and
subtracting said warped image from said second image.
2. A method as recited in claim 1, wherein obtaining said first and second images comprises:
selecting a portion of said first image using an anatomic feature in said first image;
and
selecting a portion of said second image using said anatomic feature in said second image.
3. A method as recited in claim 2, comprising:
determining a first relative area of said anatomic feature in said first image;
determining a second relative area of said anatomic feature in said second image;
selecting said first portion using said first relative area; and
selecting said second portion using said second relative area.
4. A method as recited in claim 3, wherein determining said first and second relative area comprises:
thresholding said first image to obtain corresponding first regions;
thresholding said second image to obtain corresponding second regions;
determining an area of each of said first and second regions;
determining first relative areas as a ratio of said areas of said first regions to remaining areas of said first image; and
determining second relative areas as a ratio of said areas of said second regions to remaining areas of said second images.
5. A method as recited in claim 4, wherein said matching comprises:
comparing said first and second relative areas.
6. A method as recited in claim 1, wherein said matching comprises:
determining a first relationship of an area of an anatomic feature in said first image;

determining a second relationship of an area of said anatomic feature in said second image;

determining a first average and a second average of said first and second relationships, respectively;

selecting one section of said first image corresponding to said first average; and

selecting one section of said second image corresponding to said second average.

7. A method as recited in claim 6, comprising:

selecting said one section of said first image and a number of adjacent sections of said first image as comparison sections; and

comparing each section of said comparison sections to said one section of said second image.

8. A method as recited in claim 7, comprising:

selecting a region-of-interest in each section of said comparison sections; and

cross-correlating said regions-of-interest with said one section of said second image.

9. A method as recited in claim 7, wherein said comparing comprises:

cross-correlating each section of said comparison sections with said one section of said second image.

10. A method as recited in claim 7, comprising:

matching a section from said comparison section with said one section of said second image; and

matching remaining sections of said first image with remaining sections of said second image.

11. A method as recited in claim 1, comprising:

obtaining each of said first and second images as digital images each having a plurality of pixels;

thresholding each of said first and second images to identify feature pixels corresponding to an anatomic feature;

determining a first relative area of said anatomic feature as a ratio of an area of feature pixels in said first image to an area remaining pixels in said first image;

determining a second relative area of said anatomic feature as a ratio of an area of feature pixels in said second image to an area of remaining pixels in second image; and

comparing said first and second relative areas to match said first image to said second image.

12. A method as recited in claim 11, wherein said comparing comprises:
determining a first average value of said first relative area;
determining a first portion of said first image corresponding to said first average value;

determining a second average value of said second relative area;
determining a second portion of said second image corresponding to said second relative area; and

comparing said first and second portions.

13. A method as recited in claim 1, wherein said matching comprises:
initially matching said first image to said second image; and
locally matching said first image to said second image.

14. A method as recited in claim 13, wherein said initially matching comprises:
determining whether at least one of said first and second images are rotated and whether a rotation correction is required; and
determining vertical and horizontal shifts of said first image relative to said second image.

15. A method as recited in claim 14, comprising:
using said vertical and horizontal shifts to match a section of said first image with a section of said second image; and
matching remaining sections of said first image with remaining sections of said second image in a one-to-one manner.

16. A method as recited in claim 13, wherein said locally matching comprises:
selecting a plurality of first ROIs in said first image;
selecting a plurality of second ROIs in said second image; and
determining horizontal and vertical shifts of said first ROIs in said first image relative to said second ROIs in said second image.

17. A method as recited in claim 16, comprising:
curve-fitting said horizontal and vertical shifts; and
nonlinearly warping said first image using curve-fit horizontal and vertical shifts.

18. A method as recited in claim 1, comprising:
obtaining a first CT scan as said first section images;
obtaining a second CT scan as said second section images;
selecting said first set from said first CT scan using an anatomic feature in said first CT scan; and
selecting said second set from said second CT scan using said anatomic feature in said second CT scan.

19. A method as recited in claim 18, comprising:
obtaining a first thoracic CT scan as said first CT scan; obtaining a second thoracic CT scan as said second CT scan;
selecting said first set from said first CT scan using a lung in said first CT scan; and
selecting said second set from said second CT scan using said lung in said second CT scan.

20. A method as recited in claim 19, comprising:
determining a first relative area of said lung in said first CT scan;
determining a second relative area of said lung in said second CT scan;
selecting said first set using said first relative area; and
selecting said second set using said second relative area.

21. A method as recited in claim 20, wherein determining said first and second relative area comprises:
thresholding said first CT scan to obtain first regions corresponding to said lung;
thresholding said second CT scan to obtain second regions corresponding to said lung;
determining an area of each of said first and second regions;
determining first relative areas as a ratio of said areas of said first regions to remaining areas of said corresponding first section images; and
determining second relative areas as a ratio of said areas of said second regions to remaining areas of said corresponding second section images.

22. A method as recited in claim 21, comprising:
selecting a first section of said first CT scan using said first relative areas;
selecting a second section of said second CT scan using said second relative areas; and
registering said first second and said second section.

23. A method as recited in claim 22, comprising:
selecting a plurality of sections adjacent to said first section in said first CT scan;
comparing said first section and said plurality of adjacent sections with said second section; and
matching one of said first section and said adjacent sections to said second section.
24. A method as recited in claim 23, comprising:
matching remaining sections of said first CT scan with remaining sections of said second CT scan.
25. A method as recited in claim 1, wherein said matching comprises:
determining a first area of an anatomic feature in said first image;
determining a second area of said anatomic feature in said second image;
comparing said first and second areas; and
matching said first and second images based upon said comparing.
26. A method as recited in claim 25, comprising:
selecting a first section of said first image using said first area;
selecting a second section of said second image using said second area;
comparing said first and second sections; and
matching said first and second images based upon comparing said first and second sections.
27. A method as recited in claim 26, comprising:
selecting a plurality of sections adjacent to said first section in said first image;
comparing said first section and said plurality of sections with said second section;
and
matching said first and second images based upon comparing said first section and said plurality of sections with said second section.
28. A method as recited in claim 1, comprising:
identifying an anatomic feature in each of said first and second images;
identifying respective first and second approximate middle positions of said anatomic feature in said first and second images; and
matching said first and second scans using said first and second approximate middle positions.

29. A method as recited in claim 28, comprising:
selecting a first section of said first image correspond to said first approximate middle position;
selecting a second section of said second image correspond to said second approximate middle position;
comparing said first and second sections; and
matching said first and second scans using said first and second sections.
30. A method as recited in claim 29, comprising:
selecting a plurality of sections adjacent to said first section in said first image;
comparing said first section and said plurality of sections with said second section;
and
matching said first and second images based upon comparing said first section and said plurality of sections with said second section.
31. A method as recited in claim 1, comprising:
analyzing registration of said warped image and said second image;
if said registration does not meet predetermined criteria, retrieving image data corresponding to said first image and reconstructing said first image.
32. A method as recited in claim 31, wherein analyzing said registration comprises using histogram analysis.
33. A method as recited in claim 31, comprising:
reconstructing said first image at a different reconstruction starting point;
repeating said matching, warping and subtracting steps using said first image reconstructed at said different reconstruction starting point; and
re-analyzing said registration.
34. A method as recited in claim 33, comprising:
iteratively selecting said different reconstruction starting point.
35. A method for detecting interval change, comprising:
obtaining a first image of a subject;
obtaining a second image of said subject;
matching said first and second images in a scanning direction;
detecting an interval change in matched first and second images.

36. A method as recited in claim 35, where detecting comprises:
nonlinearly warping said first image; and
subtracting a warped first image from said second image.
37. A method as recited in claim 35, comprising:
obtaining a first three-dimensional image as said first image; and
obtaining a second three-dimensional image as said second image.
38. A method as recited in claim 37, comprising:
obtaining a plurality of first section images as said first three-dimensional image;
obtaining a plurality of second section images as said second three-dimensional
image; and
matching said first and second section images along said scanning direction.
39. A method of detecting interval change, comprising:
obtaining a first scan of a subject having a plurality of sections;
obtaining a second scan of said subject having a plurality of sections;
matching three-dimensionally said first and second scans;
matching two-dimensionally corresponding sections of said first and second scans;
and
detecting an interval change between said first and second scans.
40. A method as recited in claim 39, wherein matching three-dimensionally
comprises matching said first and second scans in a scanning direction.
41. A method as recited in claim 39, comprising:
matching two-dimensionally said corresponding sections of said first and second scans
in first and second directions orthogonal to each other; and
matching three-dimensionally said first and second scans in a third direction
orthogonal to each of said first and second directions.
42. A method as recited in claim 41, wherein matching three-dimensionally
comprises matching said first and second scans in a scanning direction.
43. A method as recited in claim 39, wherein matching three-dimensionally
comprises:
identifying an anatomic feature in said first scan;
identifying said anatomic feature in said second scan; and

matching said first and second scans using said anatomic feature.

44. A method as recited in claim 43, comprising:

using said anatomic feature to select a first section of said first scan;

using said anatomic feature to select a second section of said second scan;

comparing said first and second sections; and

matching said first scan with said second scan based upon said comparing step.

45. A method as recited in claim 44, comprising:

selecting a plurality of sections adjacent to said first section in said first scan;

comparing said first section and said plurality of sections with said second section;

and

matching said first scan with said second scan based upon comparing said first section and said plurality of sections with said second section.

46. A method as recited in claim 45, comprising:

matching one of said first section and said plurality of adjacent sections with said second section; and

matching remaining sections of said first scan with remaining sections of said second scan.

47. A computer program product, comprising:

a computer storage medium and a computer program code mechanism embedded in the computer storage medium for processing an image generated in an image processing apparatus, the computer program code mechanism comprising:

a first code device configured to match first and second images of a subject in a scanning direction;

a second code device configured to detect an interval change in matched first and second images.

48. A computer program product as recited in claim 47, comprising:

a third code device configured to match three-dimensionally said first and second images; and

a fourth code device configured to match two-dimensionally corresponding sections of said first and second images.

49. A computer program product as recited in claim 47, comprising:

a third code device configured to identify an anatomic feature in said first image;
a fourth code device configured to identify said anatomic feature in said second image; and

said second code device configured to match said first and second images using said anatomic feature.

50. A computer program product as recited in claim 49, comprising:

a fifth code device configured to determine a first relative area of said anatomic feature in said first image;

a sixth code device configured to determine a second relative area of said anatomic feature in said second image;

a seventh code device configured to select a first portion of said first image using said first relative area; and

an eighth code device configured to select a second portion of said second image using said second relative area.

51. A computer program product as recited in claim 50, comprising:

a ninth code device configured to determine a first average and a second average of said first and second relative areas, respectively;

a tenth code device configured to select one section of said first image corresponding to said first average; and

an eleventh code device configured to select one section of said second image corresponding to said second average.

52. A computer program product as recited in claim 51, comprising:

said tenth code device configured to select said one section of said first image and a number of adjacent sections of said first image as comparison sections; and

a twelfth code device configured to compare each section of said comparison sections to said one section of said second image.

53. A computer program product as recited in claim 49, comprising:

a fourth code device configured to use said anatomic feature to select a first section of said first image;

a fifth code device configured to use said anatomic feature to select a second section of said second image;

a sixth code device configured to compare said first and second sections; and
said second code device configured to match said first image with said second image based upon said comparing step.

54. A computer program product as recited in claim 53, comprising:

a seventh code device configured to select a plurality of sections adjacent to said first section in said first image;

said sixth code device configured to compare said first section and said plurality of sections with said second section; and

said second code device configured to match said first image with said second image based upon comparing said first section and said plurality of sections with said second section.

55. A computer program product as recited in claim 54, comprising:

said second code device configured to match one of said first section and said plurality of adjacent sections with said second section; and

said second code device configured to match remaining sections of said first image with remaining sections of said second image.

56. A computer program product as recited in claim 47, comprising:

a third code device configured to nonlinearly warp said first image; and

a fourth code device configured to subtract a warped first image from said second image.

57. An interval change detecting system, comprising:

one of a three-dimensional image acquisition device and a three-dimensional image storage device;

a scanning direction image matching device connected to one of said image acquisition device and said image storage device;

an image subtraction device connected to said matching device.

58. A system as recited in claim 57, comprising:

said image having a plurality of sections; and

a two-dimensional image matching device connected to one of said image acquisition device and said image storage device.

59. A system as recited in claim 57, comprising:

a relative area determination circuit connected to one of said image acquisition device and said image storage device; and

a two-dimensional image matching circuit connected to said relative area determination circuit.

60. A system as recited in claim 59, comprising:

a local matching circuit connected to said two-dimensional matching circuit.

61. A system as recited in claim 60, comprising:

a warping circuit connected to said local matching circuit.

62. A system as recited in claim 60, wherein said local matching circuit comprises a cross-correlation circuit.

63. A system as recited in claim 57, comprising:

a registration analysis circuit connected to said subtraction circuit.

64. A system as recited in claim 63, wherein said registration analysis circuit comprises:

a histogram analysis circuit;

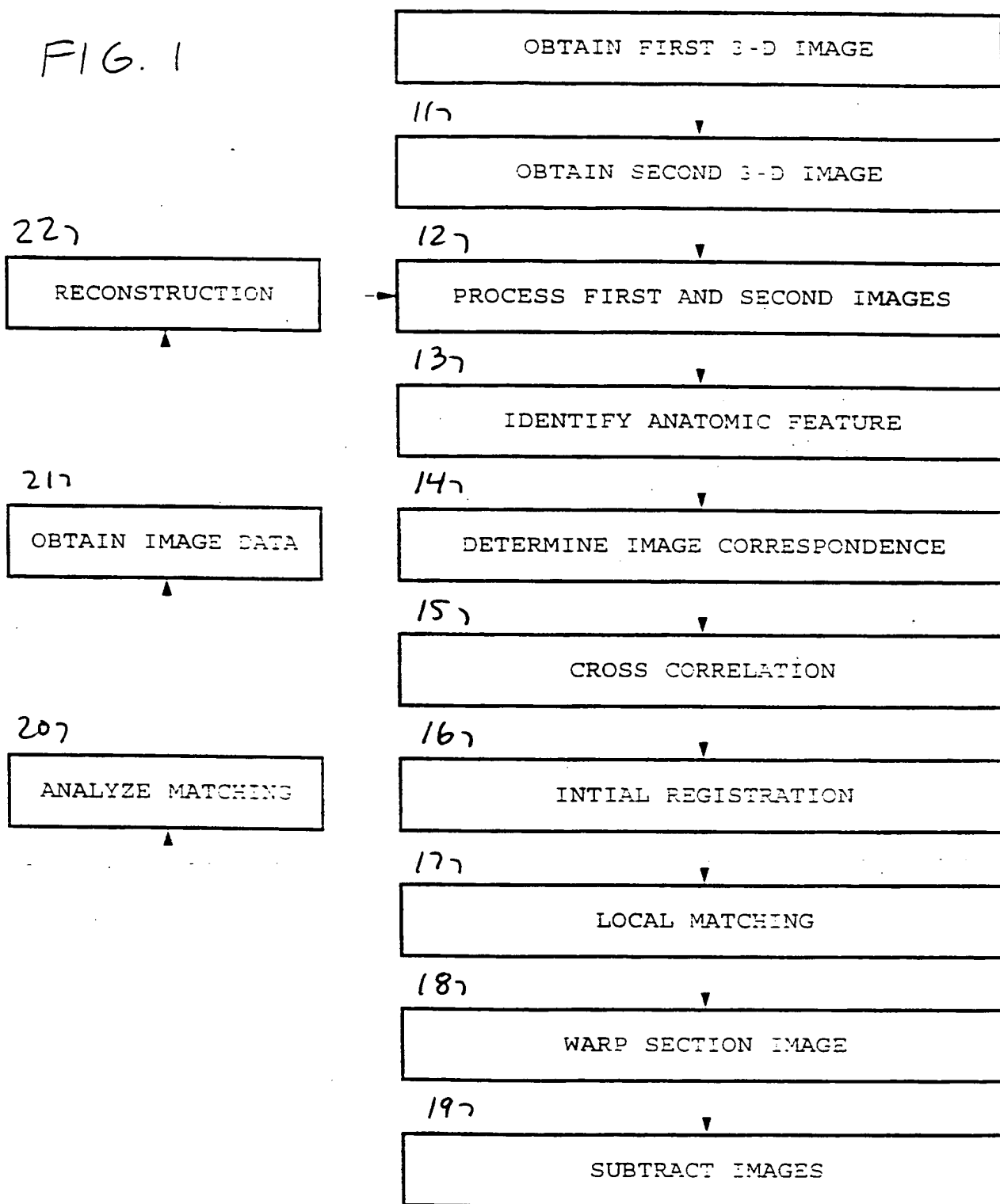
an image data retrieval circuit connected to said histogram analysis circuit; and

an image reconstruction circuit connected to said image data retrieval circuit.

1/15

107

FIG. 1



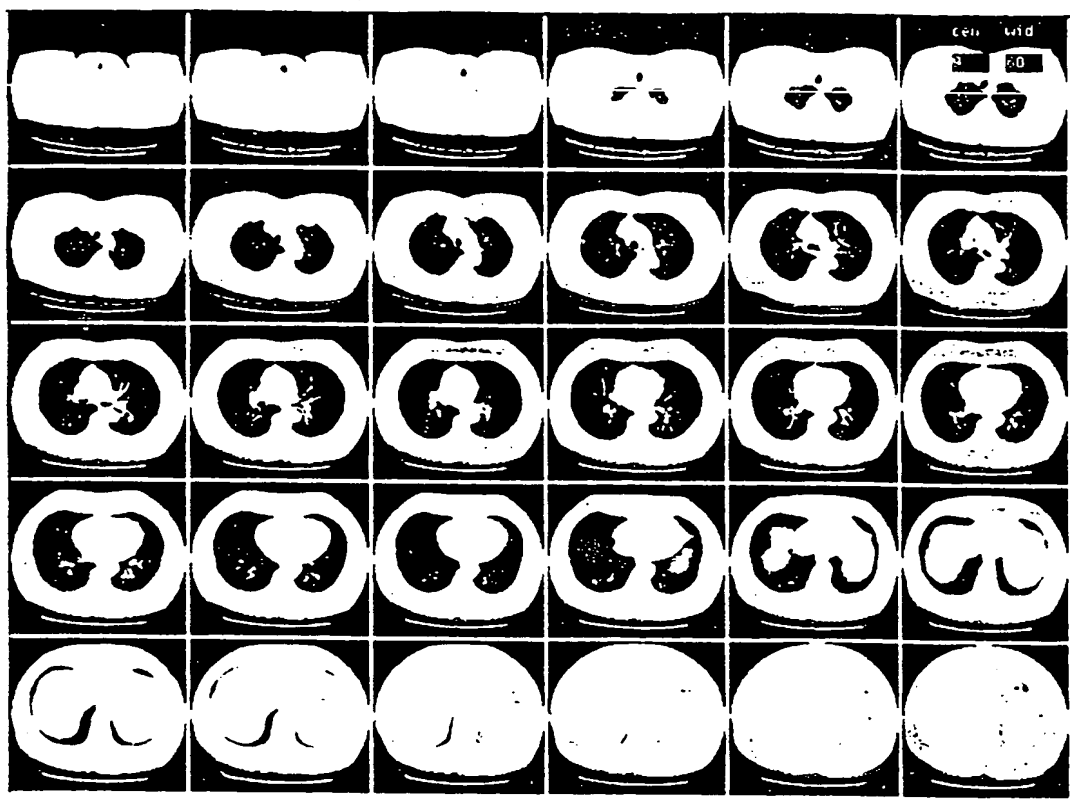


FIG. 2A

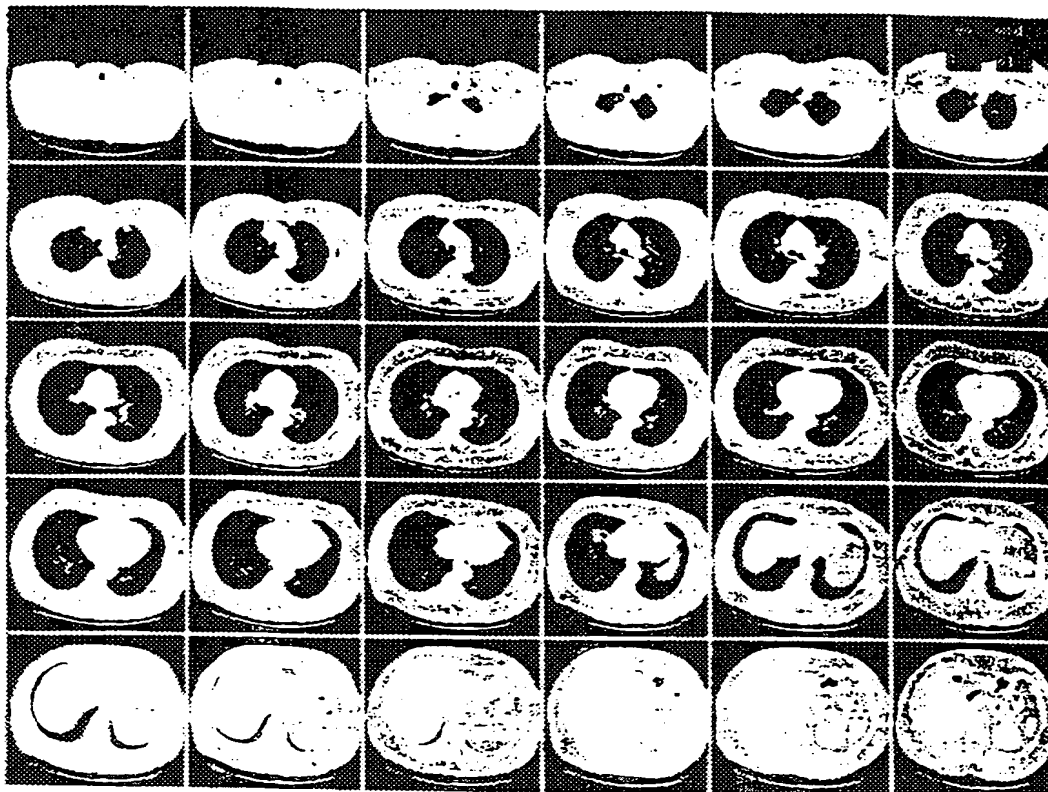


FIG. 2B

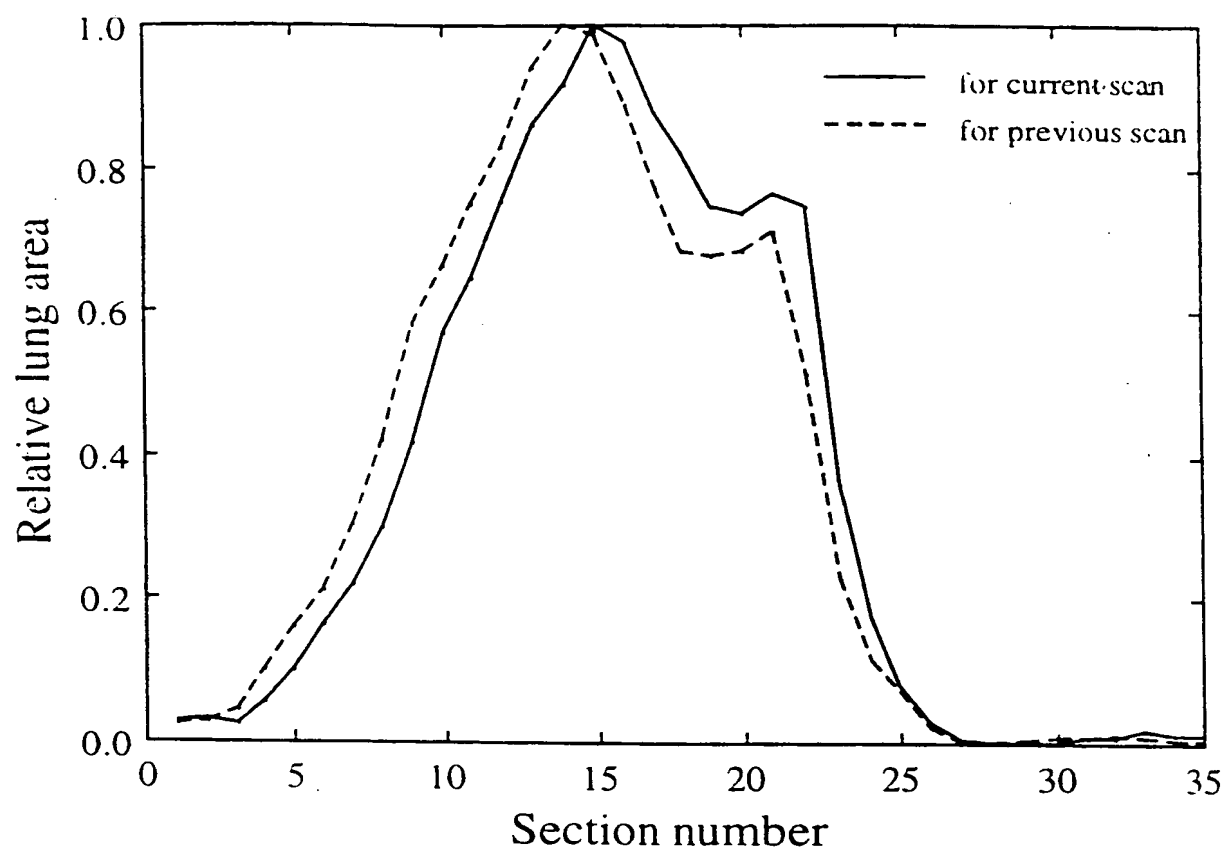


FIG. 3

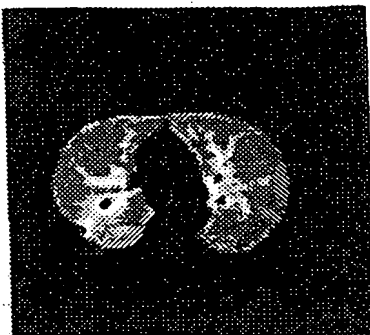


FIG. 4A



FIG. 4B



FIG. 4C

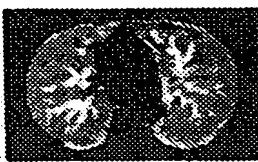


FIG. 4D



FIG. 4E



FIG. 4F

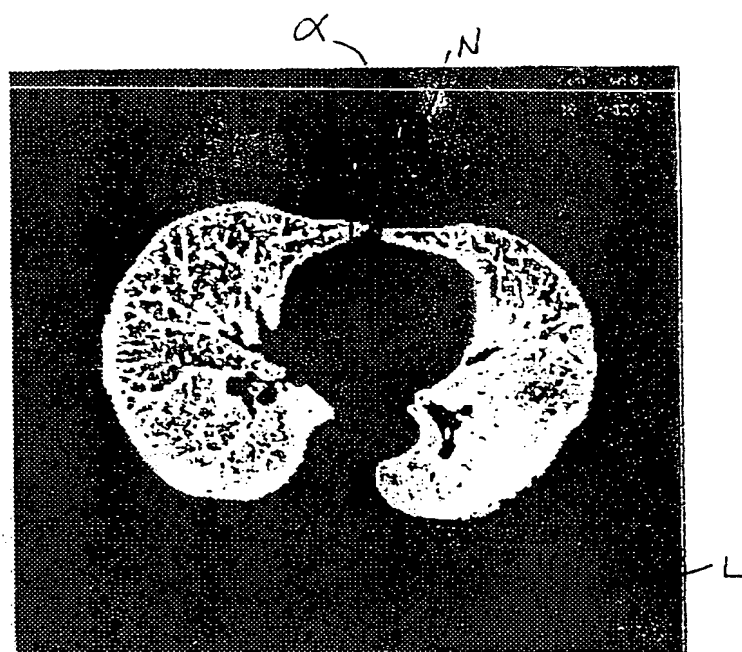


FIG. 5A

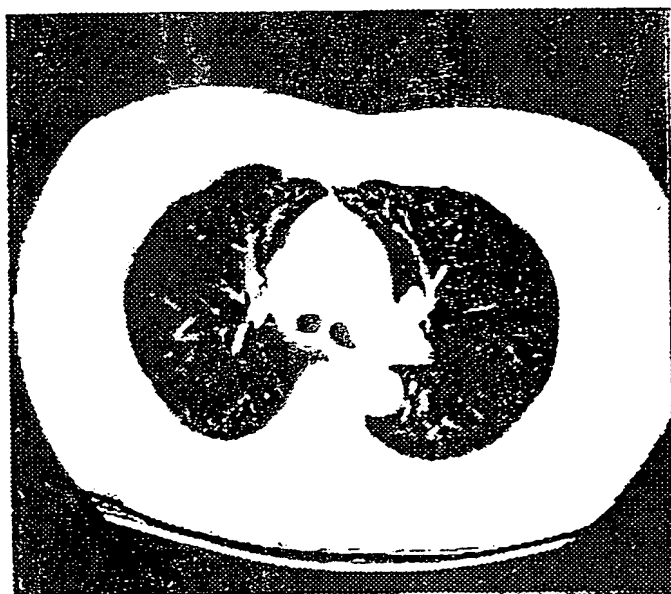


FIG. 5B

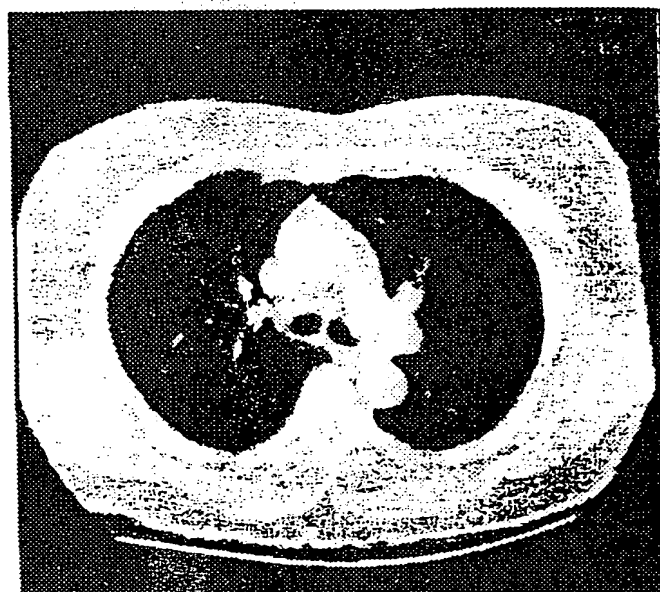


FIG. 5C



FIG. 6B

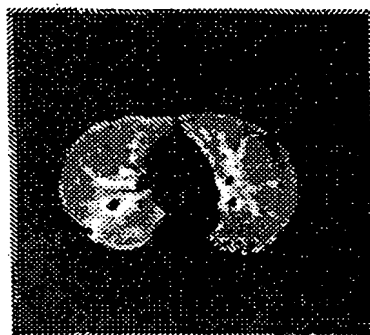


FIG. 6A

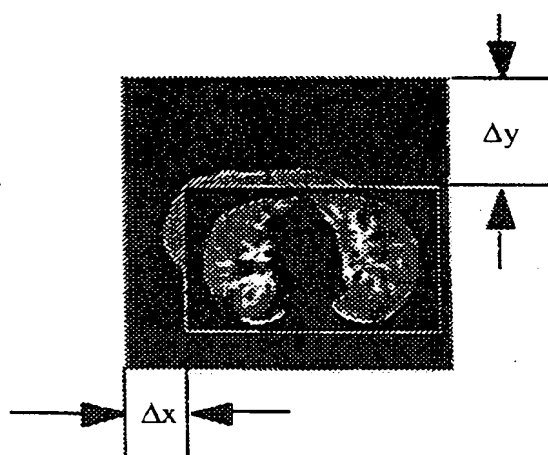


FIG. 6C

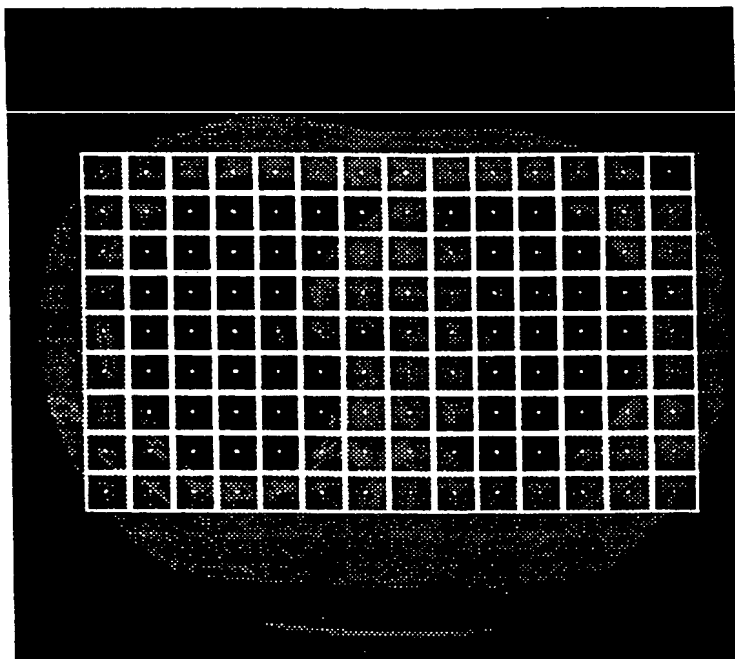


FIG. 7A

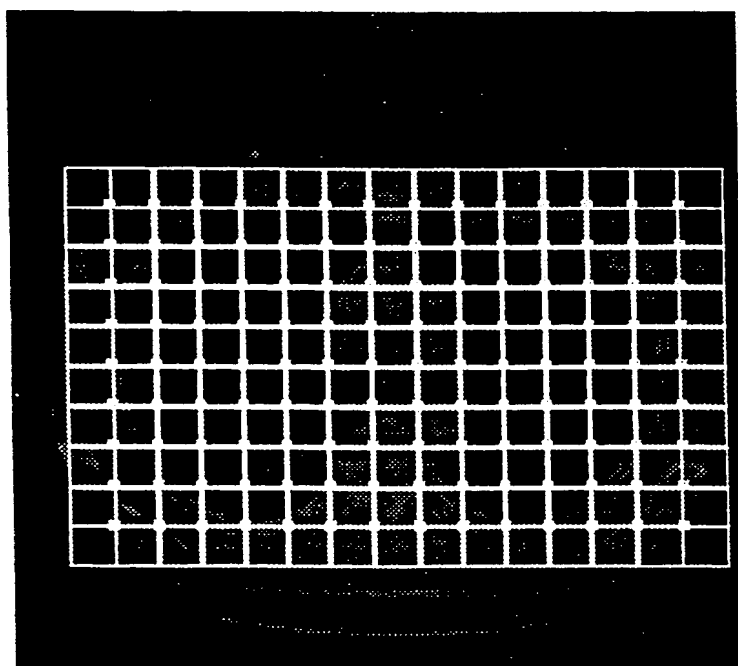


FIG. 7B

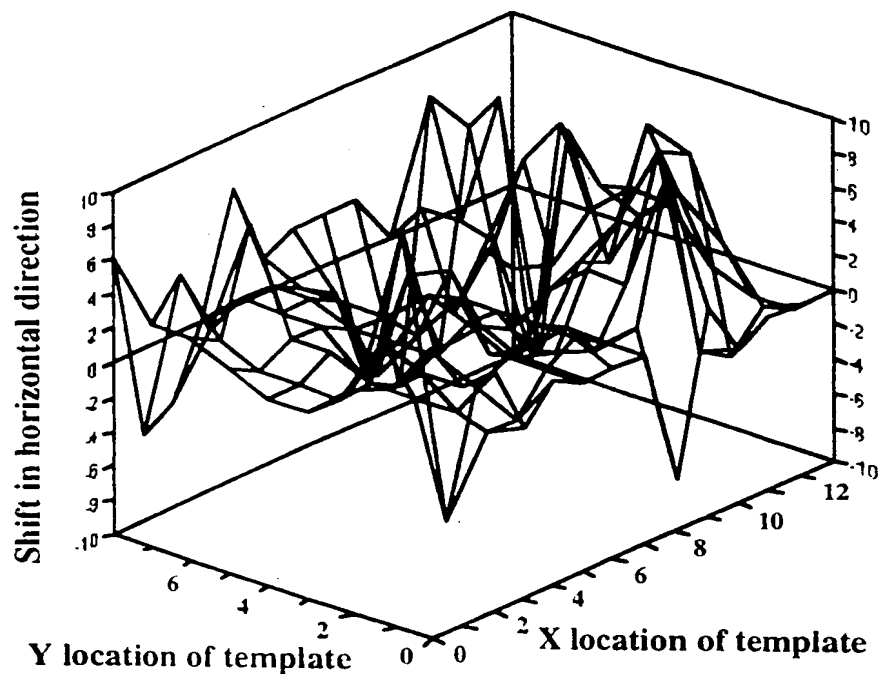


FIG. 8A

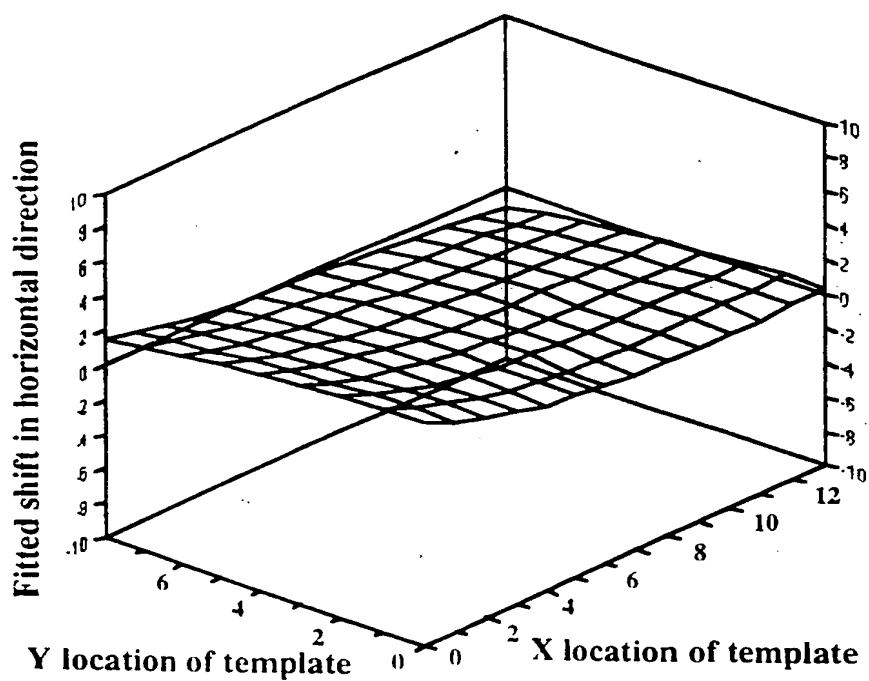


FIG. 8B

10/15

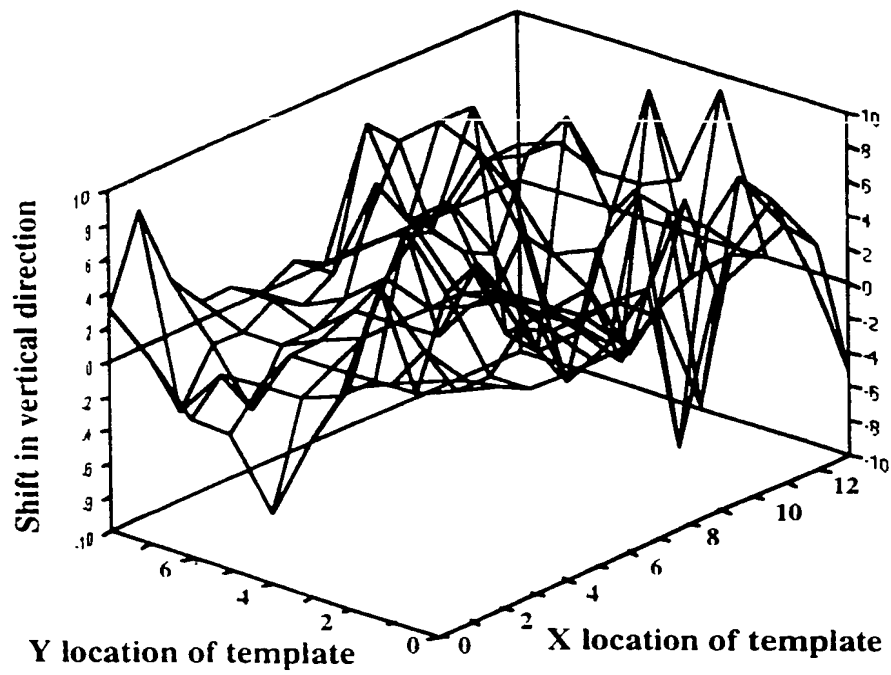


FIG. 9A

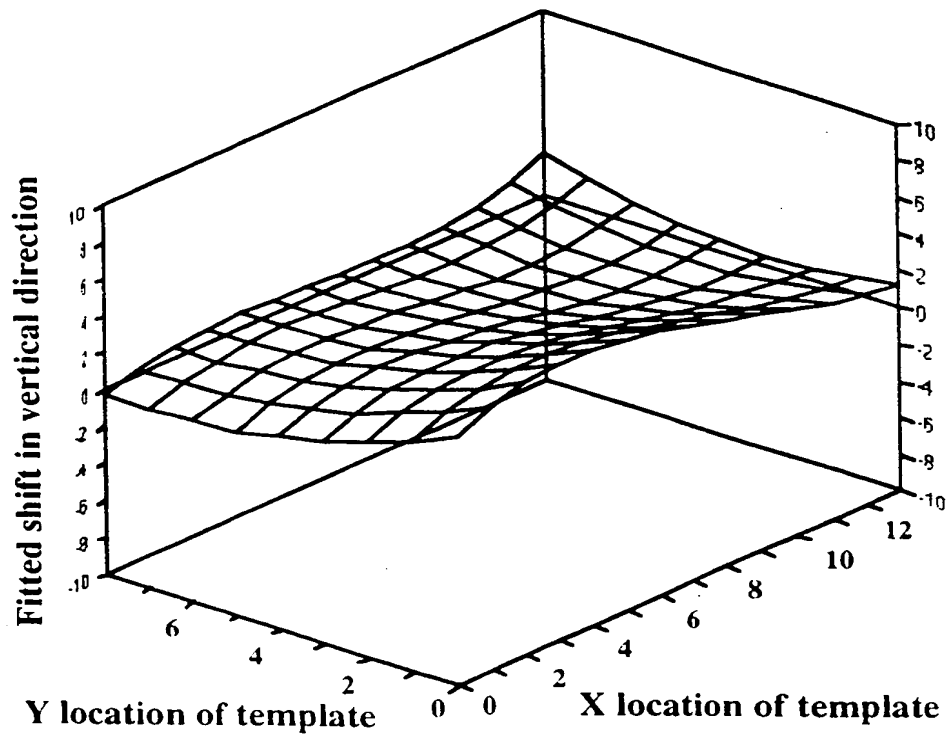


FIG. 9B



FIG. 10A

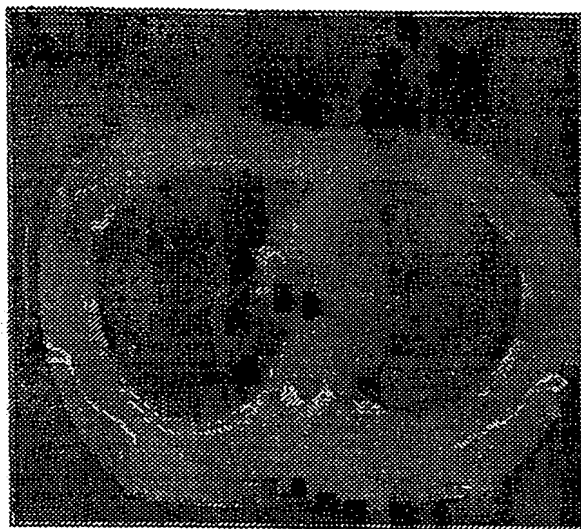


FIG. 10B

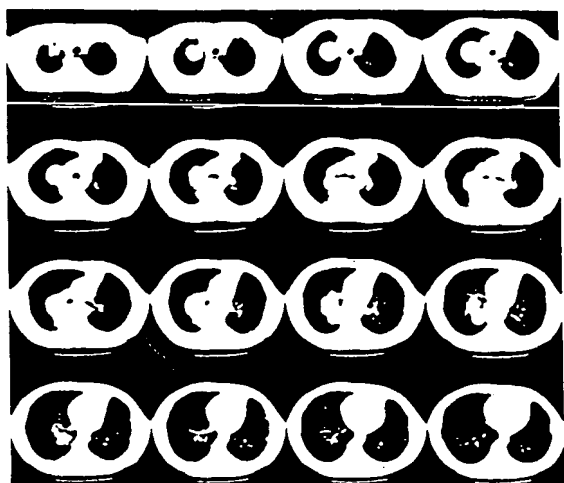


FIG. 11A

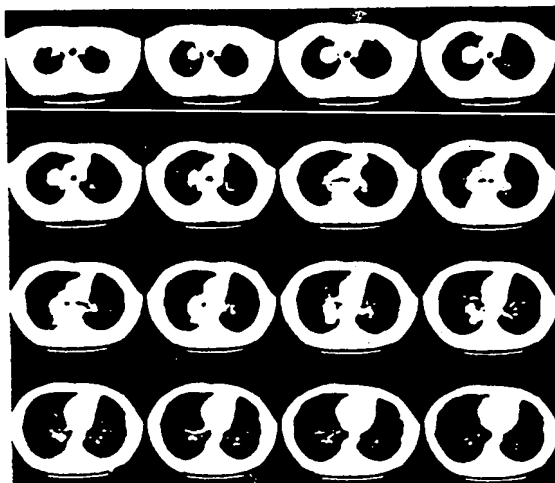


FIG. 11B

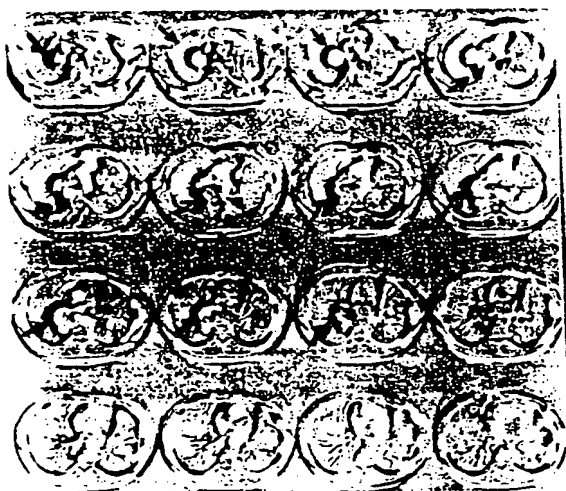


FIG. 11C

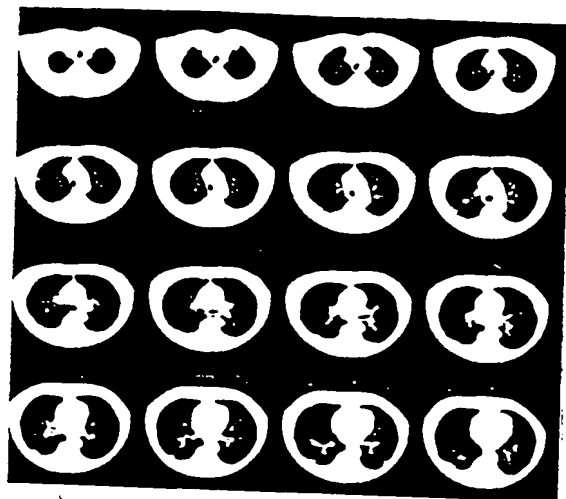


FIG. 12A

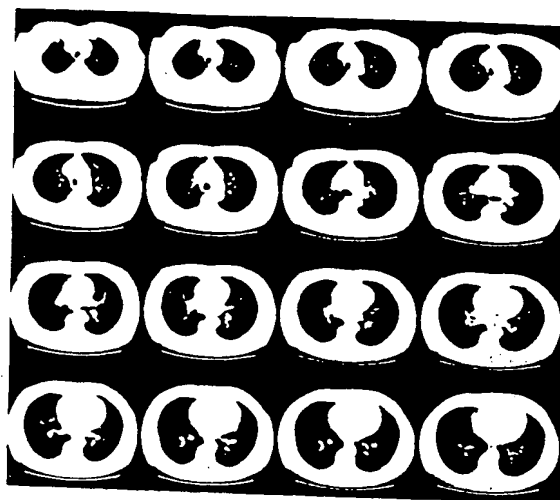


FIG. 12B

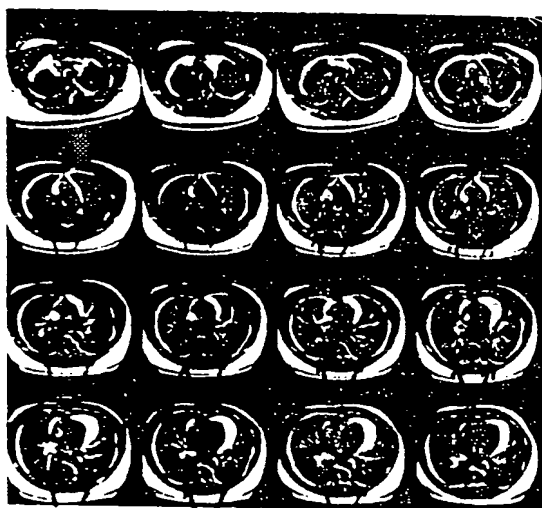


FIG. 12C

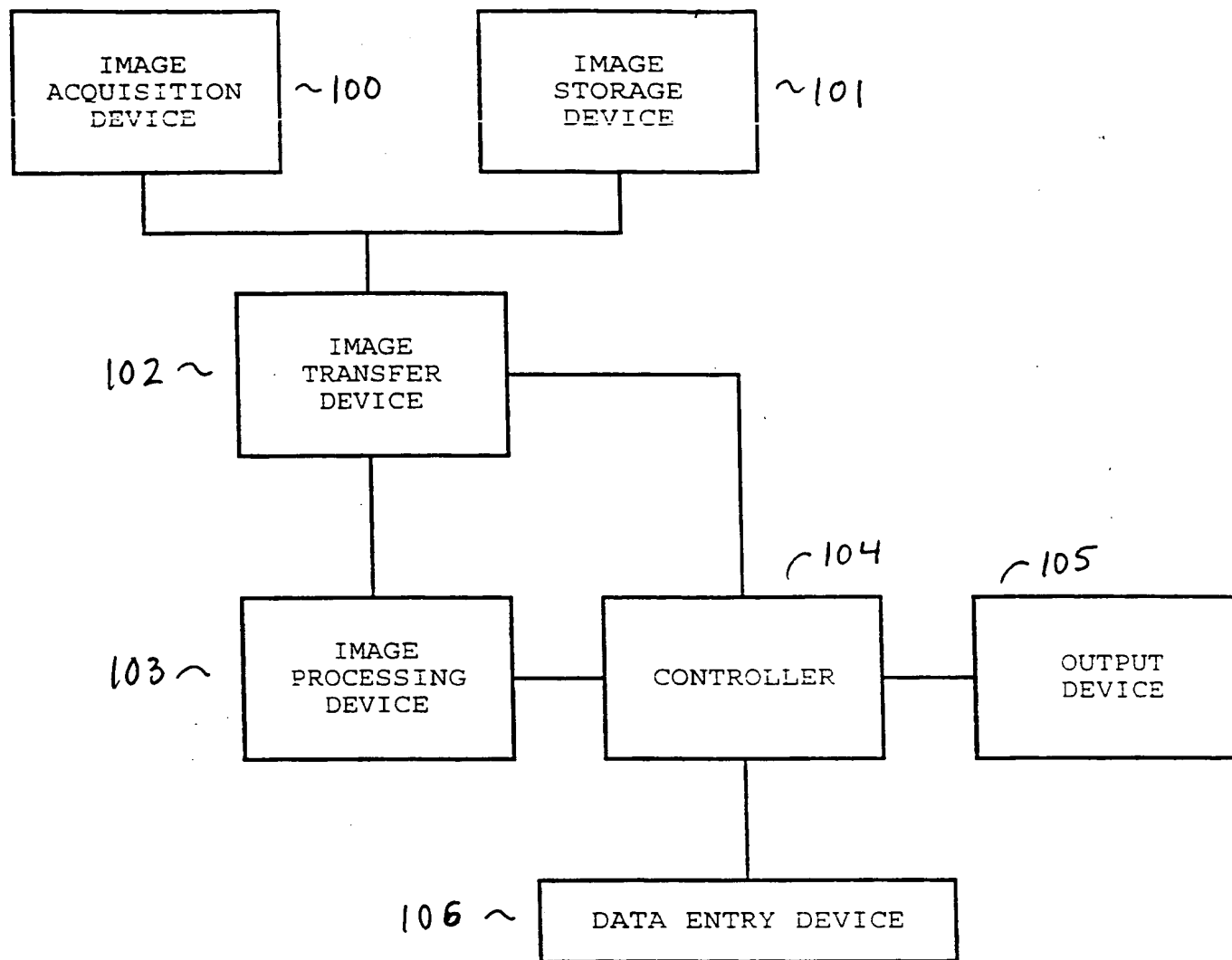


FIG. 13

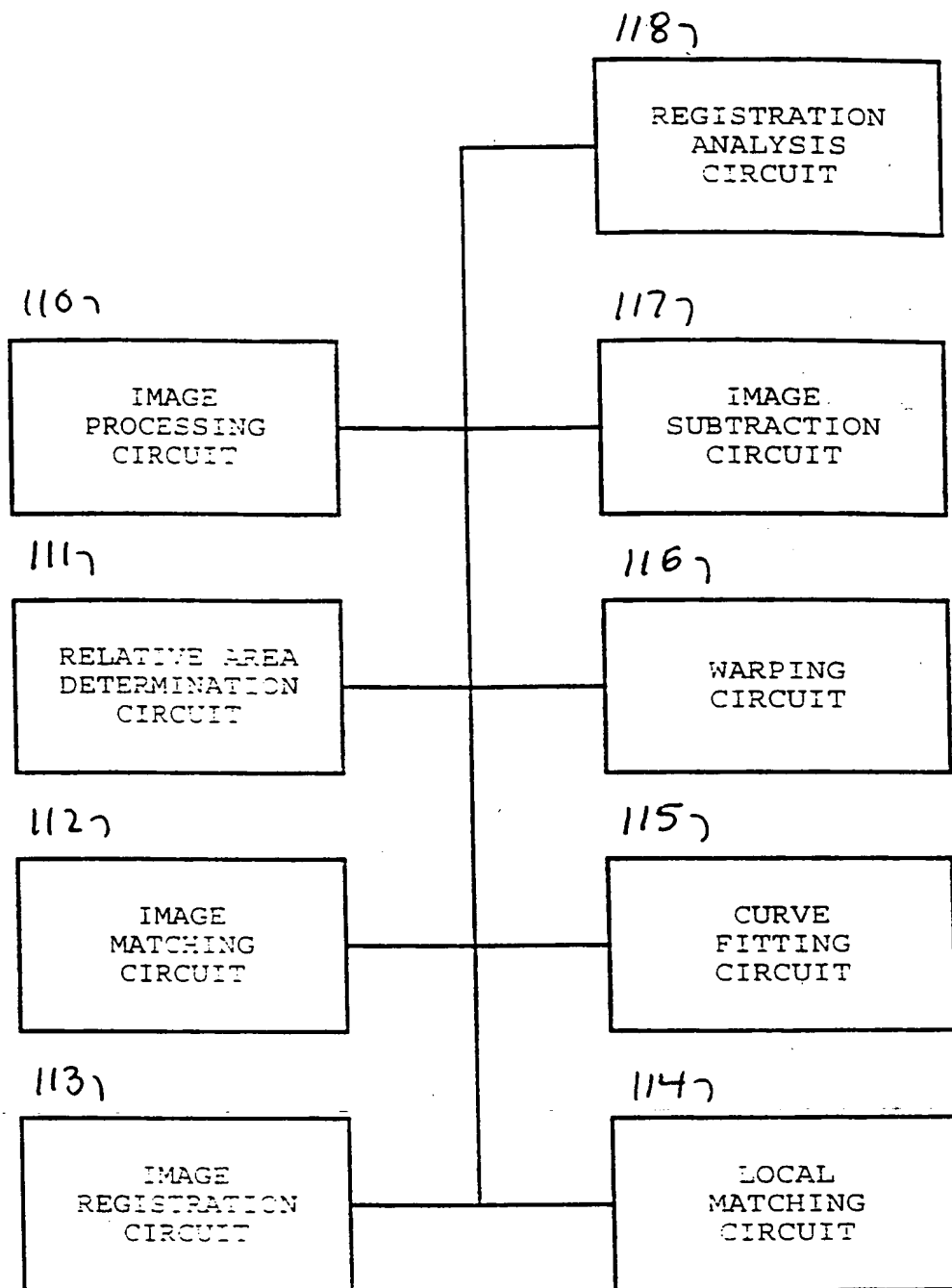
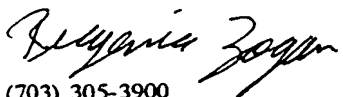


FIG. 14

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/03282

A. CLASSIFICATION OF SUBJECT MATTER IPC(6) : G06K 9/00 US CL : 382/128, 131, 294; 128/922; 378/901; 250/363.04 According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) U.S. : 382/128, 131, 294; 128/922; 378/901; 250/363.04 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) APS, CAS ONLINE		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,633,951 A (MOSHFEGHI) 27 MAY 1997, col. 2 line 23-col. 3 line 37	1-3, 18-20, 31-34, 39-44, 57-59
----- Y		----- 4-17, 21-30 35-38, 45-56, 60-64
Y	US 5,359,513 A (KANO et al.) 25 OCTOBER 1994, Figs 1b-1d col. 2 line 3-col. 3 line 29	4-17, 21-30, 35-38, 45-56, 60-64
Y	US 5,881,124 A (GIGER et al.) 09 MARCH 1999, Fig. 23 col. 2 lines 2-39	4-17, 21-30, 35-38, 45-56, 60-64
Y	US 5,319,549 A (KATSURAGAWA et al.) 07 JUNE 1994, Fig. 2A col. 2 line 12-col. 3 line 10	6-17, 35-38, 45-56, 60-64
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.		
* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art *G* document member of the same patent family	
A document defining the general state of the art which is not considered to be of particular relevance		
E earlier document published on or after the international filing date		
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)		
O document referring to an oral disclosure, use, exhibition or other means		
P document published prior to the international filing date but later than the priority date claimed		
Date of the actual completion of the international search 15 APRIL 1999	Date of mailing of the international search report 06 MAY 1999	
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer JINGGE WU  Telephone No. (703) 305-3900	

Form PCT/ISA/210 (second sheet)(July 1992) *



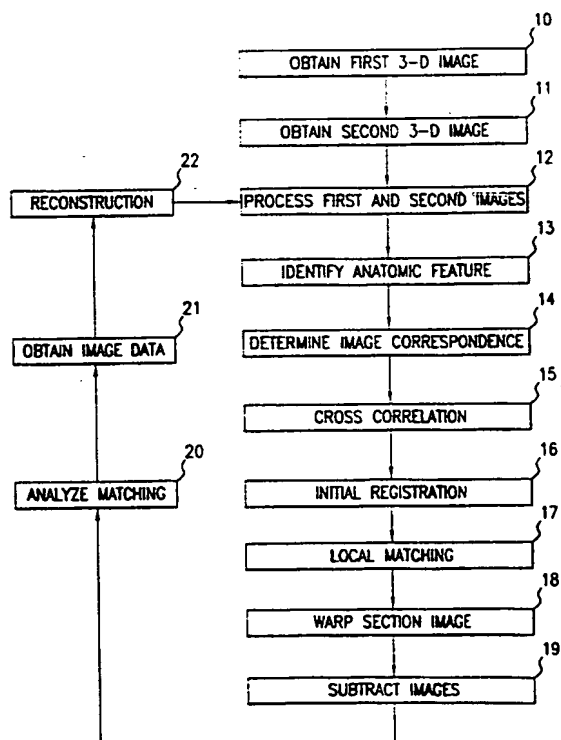
INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : G06K 9/00		A1	(11) International Publication Number: WO 99/42949
			(43) International Publication Date: 26 August 1999 (26.08.99)
(21) International Application Number: PCT/US99/03282		(81) Designated States: AU, CA, JP, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).	
(22) International Filing Date: 22 February 1999 (22.02.99)		Published <i>With international search report.</i>	
(30) Priority Data: 09/027,468 23 February 1998 (23.02.98) US			
(71) Applicant: ARCH DEVELOPMENT CORPORATION [US/US]; Room 405, 5640 South Ellis Avenue, Chicago, IL 60637 (US).			
(72) Inventors: XU, Xin-Wei; 1042 Park Crest Drive, Darien, IL 60561 (US). DOI, Kunio; 6415 Lane Court, Willowbrook, IL 60521 (US).			
(74) Agents: KUESTERS, Eckhard, H. et al.; Oblon, Spivak, McClelland, Maier & Neustadt, P.C., Suite 400, 1755 Jefferson Davis Highway, Arlington, VA 22202 (US).			

(54) Title: METHOD AND SYSTEM FOR THE AUTOMATED TEMPORAL SUBTRACTION OF MEDICAL IMAGES

(57) Abstract

Method and system for detection of interval change in medical images. Three-dimensional images, such as previous and current section images (10 and 11) in CT scans, are obtained. An anatomic feature, such as lungs, is used to select sections containing lung by a gray-level thresholding technique (13). The section correspondence between the current and previous scans is determined automatically. The initial registration of the corresponding sections in the two scans is achieved by a rotation correction (14) and a cross-correlation (15) technique. A more accurate registration between the corresponding current and previous section images is achieved by local matching (17). A nonlinear warping process (18) which is also based on the cross-correlation technique is applied to the previous image to yield a warped image after the matching. The final subtracted section images (19) were derived by subtracting of the previous section images from the corresponding current section images. Interval changes such as a change in tumor size and a newly developed pleural effusion are enhanced significantly.



FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon			PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

Method and System for the Automated Temporal Subtraction of Medical Images

CROSS-REFERENCE TO RELATED APPLICATIONS

The present is related to automated techniques for automated detection of abnormalities in digital images, for example as disclosed in one or more of U.S. Patents 4,839,807; 4,841,555; 4,851,984; 4,875,165; 4,907,156; 4,918,534; 5,072,384; 5,133,020; 5,150,292; 5,224,177; 5,289,374; 5,319,549; 5,343,390; 5,359,513; 5,452,367; 5,463,548; 5,491,627; 5,537,485; 5,598,481; 5,622,171; 5,638,458; 5,657,362; 5,666,434; 5,673,332; 5,668,888; as well as U.S. applications 08/158,388; 08,173,935; 08/220,917; 08/398,307; 5,790,690; 08/523,210; 08/536,149; 08/536,450; 5,832,103; 5,732,697; 08/562,087; 08/757,611; 08/758,438; 08/900,188; 08/900,189; 08/900,191; 08/900,192; 08/900,361; 08/900,362; 08/979,623; 08/979,639; 08/982,282; 09/028,518 and 09/027,685 each of which are incorporated herein by reference in their entirety. Of these patents and applications, 5,319,549 and 08/900,362 are of particular interest.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH

The present invention was made in part with U.S. Government support under grant numbers CA 62625 and CA 64370 (National Institutes of Health) and DAMD 71-96-6228 (U.S. Army). The U.S. Government has certain rights in the invention.

BACKGROUND OF THE INVENTION

Field of the Invention

The present invention is related to temporal analysis of medical images and, in particular, to the analysis of computed tomographic images using automated temporal subtraction.

Discussion of the Background

The application of a temporal subtraction technique to radiographic images such as chest images can significantly enhance some subtle interval changes existing in sequentially obtained images which might be missed by radiologists. These interval changes may be very important in enabling radiologists to detect some diseases, such as early lung cancer, or to assess the effects of treatment on known lesions. Difazio et al., in Digital chest radiography:

Effect of temporal subtraction images on detection accuracy, Radiology, 202:447-452 (1997) reported that the use of the temporal subtraction technique for sequential chest images can significantly increase radiologists' diagnostic accuracy in identifying interval changes.

When radiologists interpret a thoracic computed tomography (CT) scan of a patient, they commonly view it side by side with the most recent previous scan of the same patient. Such comparison readings also help radiologists to identify interval changes or to assess the effects of treatment on known lesions between two consecutive thoracic CT examinations. However, it is difficult and time-consuming for radiologists to compare current and previous (temporally sequential) thoracic CT scans to identify new findings or to assess the effects of treatments on known lesions, because this requires a systematic visual search and correlation of a large number of images (sections) in both current and previous scans. Generally, more than 25 section images were reconstructed from a thoracic CT scan with a section thickness of 10 mm. The number of section images may be much higher when a high-resolution scan (section thickness of 3 mm) is required.

Viewing several images can be difficult because of variations in the images. For example, the positioning of the patient may be different at the various times the images are produced. Patient breathing and cardiac pulsation can also produce variances in the images. It is important to be able to register images to detect interval changes where corresponding features in the images can be subtracted from each other.

The techniques for temporal subtraction, such as described in U.S. Patent 5,319,549, have only been applied to two-dimensional imaging. These techniques register and subtract two-dimensional images, such as chest radiographs.

SUMMARY OF THE INVENTION

It is an object of the present invention to provide improved automated temporal subtraction of images.

A second object of the invention is to enhance interval changes in images.

A further object of the present invention to perform automated temporal subtraction for three-dimensional scanning.

Another object of the present invention is to perform automated temporal subtraction using matching images in the direction of scanning.

A still further objection of the invention is to three-dimensionally match two images and two-dimensionally match corresponding sections of the two images.

These and other objects of the invention are achieved by a method, system and computer program product for detecting interval change in images. In the method according to the invention, first and second three-dimensional images of a subject are obtained. The first and second images are typically current and previous images of a subject. The first and second images are matched. The first image is non-linearly warped to produce a warped image and the warped image is subtracted from the second image. The subtraction can produce and/or enhance interval changes in the first and second images.

A portion of the first image may be selected using an anatomic feature in the first image. A portion of the second image may be selected using the same anatomic feature. Relative areas of the anatomic feature in the first and second images may be determined. The portions of the first and second images may be selected using the relative areas determined in the first and second images, respectively.

Determining the relative areas may be done by thresholding the first and second images to obtain corresponding regions in the first and second images. An area of each of these regions is determined and the relative areas are then determined as a ratio of an area of these regions to remaining areas in the images.

The matching of the images may be done by comparing the first and second relative areas. The matching may also be done by determining a first relationship of the area of the anatomic feature in the first and second images. Averages of the relationships of the areas can then be determined and sections of the first and second images corresponding to the averages can be selected.

It is also possible to select one section in the first image and a number of sections adjacent to that section. These sections are compared to one section selected in the second image. One of the sections selected in the first image is then matched to the section in the second image. Remaining sections in the first image may then be matched in a one-to-one manner to remaining sections and the second image.

Cross-correlation may be used in matching the images. The matching may also consist of initially matching the first image to the second image and then locally matching the first image to the second image. The initial matching may consist of determining whether the

first image is rotated and correcting the rotation, and determining vertical and horizontal shifts of the first image relative to the second image. Cross-correlation may use the vertical and horizontal shifts in matching the first and second images.

The local matching may consist of selecting regions of interest in the first and second images and determining horizontal and vertical shifts of regions of interest in the first image relative to regions of interest in the second image. The horizontal and vertical shifts may then be curve-fitted and the used in a warping process to warp the first image. The warped image may be subtracted from the second image to produce a subtracted image.

The method may also include analyzing the registration of the subtracted images. If the registration is inadequate, the image data may be retrieved and the current image may be reconstructed at a different reconstruction starting point. The analysis of the registration may be performed using histogram analysis.

The method may be advantageously applied to computed tomography (CT) scanning. In this case, the three-dimensional matching consists of matching the current and previous scans while the two-dimensional matching consists of matching the corresponding sections of the current and previous CT scans.

The invention may also be implemented in the form of a computer program product comprising a computer storage medium and a computer program code mechanism embedded in the computer storage medium. Code devices are then configured to implement various steps in detecting interval change.

These objects are also achieved by an interval change detecting system having at least one of a three-dimensional image storage device and a three-dimensional image acquisition device. A scanning direction image matching device is connected to one of the acquisition device and storage device. The system may also include a two-dimensional image matching device and a relative area determination circuit. Invention may further include a local matching circuit, a warping circuit and a cross correlation circuit. It is also possible that the system contains a registration analysis circuit which may consist of a histogram analysis circuit, an image data retrieval circuit and an image data reconstruction circuit.

BRIEF DESCRIPTION OF THE DRAWINGS

A more complete appreciation of the invention and many of the attendant advantages

thereof will be readily obtained as the same becomes better understood by reference to the following detailed description when considered in connection with the accompanying drawings, wherein:

FIG. 1 is a diagram of an embodiment of the method according to the invention;

FIGS. 2A and 2B are section images of a current thoracic CT examination by helical scanning and section images of a previous thoracic CT examination of the same patient, respectively;

FIG. 3 is a graph of the relative lung area versus section number for the CT scans shown in FIGS. 2A and 2B;

FIG. 4A is an example of a segmented, low-resolution image from the mid-section image of a current CT scan and FIGS. 4B-4F are examples of ROI images obtained from the previous scan around the mid-section, respectively;

FIG. 5A is an image illustrating the definition of the orientation of the lungs;

FIG. 5B is the image of FIG. 5A before rotation correction for lung orientation;

FIG. 5C is the image of FIG. 5A after rotation correction for lung orientation;

FIG. 6A is a section image from a current scan;

FIG. 6B is a corresponding ROI section image from a previous scan;

FIG. 6C is a diagram illustrating the definition of horizontal and vertical shifts (Δx and Δy) of the image of FIG. 6B relative to the image of FIG. 6A;

FIGS. 7A and 7B are diagrams illustrating the distribution of template ROIs on a previous section image and the distribution of search area ROIs on a current section image, respectively;

FIG. 8A is a diagram illustrating horizontal shifts (Δx) of all pairs of templates relative to the search area ROIs;

FIG. 8B is a diagram of a two-dimensional third-order polynomial fit of the horizontal shifts;

FIG. 9A is a diagram illustrating vertical shifts (Δy) of all pairs of templates relative to search area ROIs;

FIG. 9B is a diagram of a two-dimensional third-order polynomial fit of the vertical shifts;

FIG. 10A is an original section image from a previous scan;

FIG. 10B is the section image of FIG. 10A after nonlinear warping;
FIG. 11A is a diagram of section images of a current scan;
FIG. 11B is a diagram of section images of a previous scan;
FIG. 11C is a diagram of the subtracted section images obtained using the images of FIGS. 11A and 11B;
FIG. 12A is a diagram of section images of a current scan;
FIG. 12B is a diagram of section images of a previous scan;
FIG. 12C is a diagram of the subtracted section images obtained using the images of FIGS. 12A and 12B;
FIG. 13 is a diagram of the system according to the invention; and
FIG. 14 is a diagram of the image processing device according to the invention.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

With reference to the drawings, particularly FIG. 1, a first embodiment of the method according to the invention will be described. First (step 10) and second (step 11) three-dimensional images of a patient are obtained. The first and second images typically correspond to current and previous images of the same subject. The first and second images may also be two previous images of the same subject, where interval changes between the two images are desired. As an example of the invention, thoracic helical computed tomography (CT) scans of patients are obtained from a CT scanner, such as a GE HiSpeed CT/i. In CT scanning the first and second images are commonly referred to as current and previous scan. The scans are reconstructed from the image data acquired by the scanner. However, the invention is not limited to CT images. Other types of three-dimensional images, such as MRI images, may be used. The scanning pitch and section thickness for generating the CT images were 1 and 10 mm, respectively. Other values for these parameters may also be selected.

The images may be obtained directly from a scanner or may be obtained from a storage device. Typically the previous section images are from an earlier scan and have been stored. It is also not required that the images are obtained on the same or the same type of scanner. Further, the method according to the invention can also use the acquisition data (step 21) of the scans and then reconstruct the images (step 22) before further processing,

which is also described in more detail below.

In this example, the reconstructed digital section images (with DICOM header) was used. The matrix size of each reconstructed section image was 512×512 pixels. The pixel size of the section images can vary because of the different field of view (FOV) used for reconstruction in the clinical environment. The FOV for the reconstruction used in a clinical environment can vary from 29 to 42 cm. The maximum FOV allowed for reconstruction is 48 cm for the GE scanners used. In this case (including the current and previous scans), a correction factor should be applied for the FOV to all of the section images to ensure a uniform pixel size for every section image. The gray scale of the section images was 12 bits (pixel values from 0 to 4095), which corresponds to Hounsfield units (HU) of -1023 to 3072. Notice that air, water, and bone correspond to HU of -1000, 0, and 1000, respectively. In consideration of computer storage and CPU time, it is sometimes desirable to reduce the matrix size and gray scale of the thoracic CT section images to, for example, 256×256 pixels and 10 bits, respectively.

A scan for a thoracic CT examination can include a large number of section images (each with 10 mm thickness, in this example) which extend from approximately the neck of the patient down to the lower abdomen, as shown in FIGS. 2A and 2B. An interval change is usually detected by comparing anatomic features in the previous and current scans. To demonstrate the invention, the lungs were chosen as the anatomic feature in the images to be compared. However, the method is applicable to other features in the image, particularly solid organs such as the liver and kidney, or to bone and enhanced vessels.

Two pre-processing steps, i.e., segmentation of the anatomic feature and Gaussian filtering, are applied in step 12 to the first and second images. In the example, the lungs are segmented from selected sections from both the current and previous scans. The lung segmentation was achieved by use of a gray-level thresholding technique. The CT images are digital gray-scale images having a plurality of pixels (i.e., 512×512). The gray levels of the lungs corresponded generally to HU of -900 to -400. With the gray-level thresholding technique, pixels with HU above -400 and below -900 were eliminated to provide the lung area. The lung area may be approximated by a rectangle. The rectangle may be determined using horizontal and vertical profiling to detect the upper, lower and side lung edges based upon changes in pixel values. A 9×9 smooth Gaussian filter was employed to blur the vessel

structures inside the lungs.

In step 13 the portions of the images that contain the anatomic feature are identified. The portions of the images corresponding to the anatomic feature of interest, the lungs in this example, will be referred to as lung sections. For the CT images shown in FIGS. 2A and 2A, the lung sections are from section #5 to #24 and section #4 to #24, respectively. To select the lung sections from a thoracic scan, a parameter for each section in the scan is calculated, namely, the relative lung area. Here, relative lung area was defined by the ratio of the number of pixels in the section image with HU from approximately -900 to -400 to the number of remaining pixels in that section image. As mentioned above, the pixels with HU from approximately -900 to -400 mainly correspond to lung structures in the thoracic CT scan.

As mentioned above, other features such as the liver, kidney, bone or enhanced vessels may be chosen. The vessels are enhanced by injecting contrast media into the bloodstream. The image is thresholded to separate pixels corresponding to the liver or kidney, or to bone or enhanced vessel. Since these organs and features may be relatively small, it is preferable that higher resolution scanning is used with a thinner slice.

FIG. 3 shows the relative lung area plotted for each section for the two CT scans in FIGS. 2A and 2B. Obviously, the value of the relative lung area was very small (close to zero) for sections in the abdomen and neck areas. Lung sections are selected from the scan that have a certain relative lung area. In this example, a lung section was selected from the scan if the relative lung area was larger than 0.1. Other ratios may be chosen.

Once the portions of the images that contain the anatomic feature are identified, the correspondence between the first and second images is determined (step 14). The selected lung section images from both the current and previous thoracic CT scans are used to determine the section correspondence between the two scans. First the curves of relative lung area (see FIG. 3) of the two scans are generated and compared to determine, approximately, the shift in the scanning direction (i.e., in the z-axis) between the two scans (step 15). The average section number of each curve was then calculated by summation of each weighted section number with its corresponding value of the relative lung area. The average section numbers are 14.7 and 13.7 for the curves of relative lung area of the current and previous scans in FIG. 3, respectively. The difference in the average section number between the two scans is related to the starting positions in the two consecutive scans. Therefore, the

difference between the two average section numbers indicated the overall shifts in the scanning direction (i.e., in the z-axis) between the two scans. Intuitively, for the same patient, if the table position and the patient scanning starting position were kept the same in the two consecutive scans, then the two curves of the relative lung area should match exactly, and the two average section numbers should be the same. However, it is very difficult to keep these positions unchanged in a clinical environment.

In the two images a point is selected as an initial benchmark for finding the correspondence between the two images. For the thoracic CT scan example, the section image whose section number equals the nearest integer of its average section number is defined as the mid-section image of the scan. The mid-sections of the current and previous scans were used as the initial benchmark. The mid-section and several adjacent sections (two above and two below, a total of five sections, for example) are selected from the previous scan for comparison, one by one, with the mid-section from the current scan to find a pair of the best-matched section images in the two scans at the region around the mid-lung. For this comparison, the matching of the overall lung shape is more important than the detailed structures, such as vessels in the lungs.

A cross-correlation technique is used (step 15) to compare the mid-section image of the current scan to each of the selected (five) section images of the previous scan. To apply the cross-correlation technique, region-of-interest (ROI) images selected from the five section images of the previous scan are used instead of the section images themselves. Each ROI image has a width and height large enough to encompass the lungs for each section. In this example, the width and height of the ROI are 200 and 126 pixels, respectively. The center of the ROI for a section image is selected as the center of the lung area of that section image. FIG. 4A is an example of a section image while FIGS. 4B-4F are examples of the ROI section images selected for this comparison.

The normalized cross-correlation values between the mid-section of the current scan and each of the five ROIs of the previous scan were then calculated. The pair of sections which provided the highest cross-correlation value was identified as the corresponding section pair between the current and previous scans. The remaining sections in both scans were then correlated rigidly based on the determined corresponding pair with the highest cross-correlation value, i.e., in a one-to-one manner. Any remaining unpaired sections are

ignored for further processing.

In a three-dimensional scan, such as a CT scan, a number of sections or slices are reconstructed. These slices is generally treated as having x-axis and y-axis data, while the scanning is preformed in the z-axis direction. Thus, the present invention matches corresponding sections or slices in the previous and current images two-dimensionally, in the x- and y-axis directions, and matches the scans (containing a number of section or slices) three-dimensionally in the z-axis direction.

After the establishment of the one-to-one section correspondence in the current and previous images, i.e. matching in the scanning direction (three-dimensional matching), the initial registration of the paired section images is performed in step 16 (two-dimensional matching). For the CT sections, each pair of corresponding section images in the two scans are initially registered. The initial registration of the corresponding section images in the two scans included two steps: a rotation correction and the determination of vertical and horizontal shifts of the previous section image relative to the current section image. The lungs in the thoracic CT section images were often oriented toward the right or left side because of patient movement, breathing, and lying on the back improperly during the scanning. FIG. 5A illustrates a section image with the lungs oriented to the left side. Commonly, the lung orientation is only slightly different for different sections in a given scan. However, the difference in lung orientations could be very large for sections from different scans.

The lung orientation is defined by the angle (α) between the vertical axis (Y axis) of the section image and the normal line (N) to the line segment (L) which goes through the lowest points in each lung, as illustrated in FIG. 5A. The orientation of each section image in both the current and previous scans was determined and corrected using known techniques. FIGS. 5B and 5C show an example of before and after the rotation correction for the orientation of the section image of FIG. 5A.

The relative shifts in the vertical and horizontal directions between the previous section image and the corresponding current section image were determined also by use of the cross-correlation technique with the segmented, low-resolution images, as shown in FIG. 6. The similar ROI image (200×126 pixels, including the entire lungs) from the previous section image was again used for this purpose. The ROI image was moved through the current

section image pixel by pixel, and the normalized cross-correlation value at each pixel was obtained. The horizontal and vertical shifts (Δx and Δy) of the previous section image relative to the current section image were determined when the cross-correlation value reached its maximum value, as shown in FIG. 6B.

After the process of initial registration, local matching is applied to the images to obtain more accurate registration (step 17). For the CT scans, the corresponding pair of sections of the current and previous scans are locally matched. The local matching technique is again based on the cross-correlation technique, which results in nonlinear warping of the previous section image. To perform the local matching, many small ROIs were selected automatically over the lung area of the section image, as shown in FIGS. 7A and 7B. Recall that the lung area in the section image was approximated by a rectangle. An ROI selected in the previous section image is called a template ROI (or simply a template), and that selected in the current section image is called the search area ROI. The sizes of the template and search area ROIs were 16×16 and 32×32 pixels, respectively. Other sizes may be used. The distance between the centers of the two adjacent ROIs was fixed as 16 pixels for both the template and search area ROIs. For each pair of template and search area ROIs, the template was moved through the search area ROI pixel by pixel. The normalized cross-correlation value at each pixel was calculated. The maximum value of the cross-correlation indicated that the subregion in the search area ROI where the template overlapped was the "best" match with the template. The assignment of the template and search ROIs could be reversed, i.e., the search ROI could be selected in the previous section image.

The horizontal and vertical shifts (Δx and Δy) between the center of the template and the center of the search area ROI for the best match was thus determined. FIGS. 8A and 9A indicate the distributions of the shift values Δx and Δy , respectively, derived for all pairs of template and search area ROIs in FIGS. 7A and 7B. It should be noted that the local matching should be limited to the area of the anatomic feature in the images (i.e., the lung area in the section images).

A two-dimensional curve fitting with third-order polynomials, based on a least-squares method, was used for fitting Δx and Δy in order to obtain the continued shift values at each pixel for the purpose of nonlinear warping of the previous section image. Other curve fitting techniques may also be used. FIGS. 8B and 9B illustrate the fitted shift

values of Δx and Δy , respectively, at every pixel of the previous section image within the lung area, as shown in FIGS. 7A and 7B.

To obtain the subtracted section image between the current and previous sections, the previous section image was warped (step 18) and then subtracted (step 19) from the current section image. The warping of the previous section image is based on the fitted shift values, as described in detail U.S. 5,319,549, application Serial No. 08/900,362, and Kano et al., *Digital image subtraction of temporally sequential chest images for detection of interval change*, Med Phys, vol. 2, No. 1 pp. 453-461 (1994). FIGS. 10A and 10B illustrate a previous section image and its warped image.

EXAMPLE

A total of 14 cases (14 pairs of temporally sequential thoracic CT scans) were used to demonstrate the method according to the invention. The time interval between the current and previous thoracic CT scans was varied from two to seven months. The truth of the presence or absence of interval changes was obtained by an experienced radiologist reading the images. Two cases were reported to have interval changes, and the other cases had no interval changes, according to the radiologists.

FIGS. 11A-11C show the case in which an anterior mediastinal mass (at the left side in the section images) increased in size from 3 cm in the previous scan to 4 cm in the current scan. On the subtracted section images (FIG. 11C), the dark area surrounding the mass indicates that the mass is increased in size. The dark area is indicated by the arrows. With the method according to the invention, the new findings or interval changes in the current sections are shown as dark patterns on the subtracted section images. Also, for this case, the right hilar region had increased in size in the current section images; this was again shown as a dark region in the subtracted section images, as also seen in FIG. 11C.

FIGS. 12A-12C show another case of temporal subtraction, in which a new pleural effusion (indicated by the arrows in FIG. 12C) developed at the lung bases in the current section images. The newly developed pleural effusion may be due to metastatic disease or to another cause. On the subtracted section images (FIG. 12C), the dark structures with a waning moon shape in the left and right lower parts of the lungs illustrate the newly developed symptom.

It will be noted that some vascular structures remained in the subtracted section

images. The main reason for misregistration of these vascular structures in the current and previous sections was probably the partial volume effect due to the variation in the depth of patient inspiration during the scan, and also to the different starting positions for the scans in the two sequential CT examinations. Although it is difficult to control patient breathing in different scans, it is possible to overcome the partial volume effect caused by the different starting positions in two sequential scans, if the raw data from the helical scanning are available.

In a modification of the method according to the invention, the raw scanning data are obtained (step 19) and the section images of a helical scan can be reconstructed for different starting locations on the z-axis from the data (step 20). In the clinical situation, the reconstruction usually starts at the position where the scanning starts physically. The registration of the corresponding sections in two scans can be greatly improved if the reconstruction starting position of one scan can be properly adjusted within the range of one section thickness (i.e., 10 mm in this example), with an accuracy on the order of 1 mm. Whether to use the raw data to reconstruct the images may be determined using histogram analysis and subtracted image to determine the degree of misregistration. The histogram has a broader distribution when there is misregistration since there are more light and dark patterns in the subtracted image. On the other hand, the histogram has a narrower distribution when there are fewer light and dark patterns. A measure of the breadth or narrowness of the histogram may be used to automatically determine if the registration is acceptable.

If the histogram analysis shows that there is significant misregistration, the current image may be reconstructed using a different starting point. The new starting point can be determined iteratively by shifting the previous starting point by a fixed distance, such as 1 mm. The scanner has the capability of image reconstructing based on a number of input parameters, including starting a reconstruction at any point with a section. The input parameters may be adjusted to produce a better match of the current and previous images. The method according to the invention is repeated with the newly reconstructed images. When the registration is found to be acceptable using the histogram analysis, the images can be output.

FIG. 13 is a diagram of the system according to the invention. Images (or data) is obtained from image acquisition device 100 and image storage device 101. Image

acquisition device 100 may be a CT scanner or an MRI scanner, for example. Image storage device 101 may be a memory device, an optical disk reader, when the images or data are stored on optical disk, or the PACS system (picture archiving communication system) where the images are usually stored on magnetic tape. An image transfer device 102 transfers images from devices 100 and 101 to image processing device 103. Device 103 carries out the operations described above in connection with the method embodiment. For example, device 103 processes the image by conducting the thresholding operation on the images and the Gaussian filtering. Device 103 also performs the relative area determinations, matching and cross-correlations, as well as the warping and subtracting. Device 103 may contain memory to store data or images on which the operations are being carried out, or intermediate results.

Devices 100-103 are controlled by a controller 104. Controller 104 may be, for example, a computer. Controller 104 also controls the output or display of the results of device 103 sent to output device 105. Output device 105 may be a video display terminal or a printer. A data entry device 106, such as a keyboard and pointing device, is provided to enter commands for the controller 104 to control the various devices to carry out the operations on the images or image data.

The system according to the invention may also be implemented in software run on a computer. Software code devices maybe written to carry out the various operations on the images. Thus, the invention may also be implemented as a program embedded in a computer-readable storage medium, such as a magnetic or optical disk.

FIG. 14 is a more detailed diagram of device 103. Device 103 includes an image processing circuit 110 that performs thresholding and, if needed, filtering operations or other desired image processing. The image after processing by circuit 110 used by circuit 111 to determine the relative area of an anatomic feature, such as the lungs. Image matching circuit 112 performs the cross-correlation to determine the initial registration of the two images, and ROI selection in the images for this operation. In the CT example, the mid-section image from the current is compared with the five selected section images from the previous scan using the cross-correlation operation to match the two scans.

Image registration circuit 113 performs the rotation correction and the determination of the vertical and horizontal shifts, using the matched images.

Local matching circuit 114 locally matches the images (the section pairs in the CT

example) for accurate registration. Template and search ROIs are selected and the distribution of the horizontal and vertical shifts are determined using cross-correlation.

A curve-fitting circuit 115 fits the distribution of the horizontal and vertical shifts using a polynomial fit, as discussed above. The fitted distribution is used by warping circuit 116 to produce the warped image, which is subtracted by subtraction circuit 117 from the current image to produce the subtracted images.

The circuit may also contain a registration analysis circuit 118 that determines if the registration is acceptable. If the registration is not found to be acceptable, using histogram analysis, for example, the circuit causes the system to obtain the image data (CT scanning data in this example) and the data is used by the image acquisition device to reconstruct the section images at a more desired starting point to eliminate image artifacts such as the partial volume artifact. This operation may be done iteratively.

The automated registration and subtraction method and system according to the invention, particularly when applied to temporally sequential section images, can enhance some interval changes effectively, such as changes in tumor size and the development of new nodules and pleural effusions. Therefore, the method and system according to the invention may help radiologists to identify and assess subtle interval changes in thoracic CT examinations more quickly and accurately.

Obviously, numerous modifications and variations of the present invention are possible in light of the above teachings. It is therefore to be understood that within the scope of the appended claims, the invention may be practiced otherwise than as specifically described herein.

Claims:

1. A method for detecting interval change, comprising:
obtaining a first three-dimensional image of a subject;
obtaining a second three-dimensional image of said subject;
matching said first and second images;
nonlinearly warping said first image to produce a warped image; and
subtracting said warped image from said second image.
2. A method as recited in claim 1, wherein obtaining said first and second images comprises:
selecting a portion of said first image using an anatomic feature in said first image;
and
selecting a portion of said second image using said anatomic feature in said second image.
3. A method as recited in claim 2, comprising:
determining a first relative area of said anatomic feature in said first image;
determining a second relative area of said anatomic feature in said second image;
selecting said first portion using said first relative area; and
selecting said second portion using said second relative area.
4. A method as recited in claim 3, wherein determining said first and second relative area comprises:
thresholding said first image to obtain corresponding first regions;
thresholding said second image to obtain corresponding second regions;
determining an area of each of said first and second regions;
determining first relative areas as a ratio of said areas of said first regions to remaining areas of said first image; and
determining second relative areas as a ratio of said areas of said second regions to remaining areas of said second images.
5. A method as recited in claim 4, wherein said matching comprises:
comparing said first and second relative areas.
6. A method as recited in claim 1, wherein said matching comprises:
determining a first relationship of an area of an anatomic feature in said first image;

determining a second relationship of an area of said anatomic feature in said second image;

determining a first average and a second average of said first and second relationships, respectively;

selecting one section of said first image corresponding to said first average; and

selecting one section of said second image corresponding to said second average.

7. A method as recited in claim 6, comprising:

selecting said one section of said first image and a number of adjacent sections of said first image as comparison sections; and

comparing each section of said comparison sections to said one section of said second image.

8. A method as recited in claim 7, comprising:

selecting a region-of-interest in each section of said comparison sections; and

cross-correlating said regions-of-interest with said one section of said second image.

9. A method as recited in claim 7, wherein said comparing comprises:

cross-correlating each section of said comparison sections with said one section of said second image.

10. A method as recited in claim 7, comprising:

matching a section from said comparison section with said one section of said second image; and

matching remaining sections of said first image with remaining sections of said second image.

11. A method as recited in claim 1, comprising:

obtaining each of said first and second images as digital images each having a plurality of pixels;

thresholding each of said first and second images to identify feature pixels corresponding to an anatomic feature;

determining a first relative area of said anatomic feature as a ratio of an area of feature pixels in said first image to an area remaining pixels in said first image;

determining a second relative area of said anatomic feature as a ratio of an area of feature pixels in said second image to an area of remaining pixels in second image; and

comparing said first and second relative areas to match said first image to said second image.

12. A method as recited in claim 11, wherein said comparing comprises:
determining a first average value of said first relative area;
determining a first portion of said first image corresponding to said first average value;

determining a second average value of said second relative area;
determining a second portion of said second image corresponding to said second relative area; and

comparing said first and second portions.

13. A method as recited in claim 1, wherein said matching comprises:
initially matching said first image to said second image; and
locally matching said first image to said second image.

14. A method as recited in claim 13, wherein said initially matching comprises:
determining whether at least one of said first and second images are rotated and whether a rotation correction is required; and

determining vertical and horizontal shifts of said first image relative to said second image.

15. A method as recited in claim 14, comprising:
using said vertical and horizontal shifts to match a section of said first image with a section of said second image; and
matching remaining sections of said first image with remaining sections of said second image in a one-to-one manner.

16. A method as recited in claim 13, wherein said locally matching comprises:
selecting a plurality of first ROIs in said first image;
selecting a plurality of second ROIs in said second image; and
determining horizontal and vertical shifts of said first ROIs in said first image relative to said second ROIs in said second image.

17. A method as recited in claim 16, comprising:
curve-fitting said horizontal and vertical shifts; and
nonlinearly warping said first image using curve-fit horizontal and vertical shifts.

18. A method as recited in claim 1, comprising:
obtaining a first CT scan as said first section images;
obtaining a second CT scan as said second section images;
selecting said first set from said first CT scan using an anatomic feature in said first CT scan; and
selecting said second set from said second CT scan using said anatomic feature in said second CT scan.

19. A method as recited in claim 18, comprising:
obtaining a first thoracic CT scan as said first CT scan; obtaining a second thoracic CT scan as said second CT scan;
selecting said first set from said first CT scan using a lung in said first CT scan; and
selecting said second set from said second CT scan using said lung in said second CT scan.

20. A method as recited in claim 19, comprising:
determining a first relative area of said lung in said first CT scan;
determining a second relative area of said lung in said second CT scan;
selecting said first set using said first relative area; and
selecting said second set using said second relative area.

21. A method as recited in claim 20, wherein determining said first and second relative area comprises:
thresholding said first CT scan to obtain first regions corresponding to said lung;
thresholding said second CT scan to obtain second regions corresponding to said lung;
determining an area of each of said first and second regions;
determining first relative areas as a ratio of said areas of said first regions to remaining areas of said corresponding first section images; and
determining second relative areas as a ratio of said areas of said second regions to remaining areas of said corresponding second section images.

22. A method as recited in claim 21, comprising:
selecting a first section of said first CT scan using said first relative areas;
selecting a second section of said second CT scan using said second relative areas; and
registering said first second and said second section.

23. A method as recited in claim 22, comprising:
selecting a plurality of sections adjacent to said first section in said first CT scan;
comparing said first section and said plurality of adjacent sections with said second section; and
matching one of said first section and said adjacent sections to said second section.
24. A method as recited in claim 23, comprising:
matching remaining sections of said first CT scan with remaining sections of said second CT scan.
25. A method as recited in claim 1, wherein said matching comprises:
determining a first area of an anatomic feature in said first image;
determining a second area of said anatomic feature in said second image;
comparing said first and second areas; and
matching said first and second images based upon said comparing.
26. A method as recited in claim 25, comprising:
selecting a first section of said first image using said first area;
selecting a second section of said second image using said second area;
comparing said first and second sections; and
matching said first and second images based upon comparing said first and second sections.
27. A method as recited in claim 26, comprising:
selecting a plurality of sections adjacent to said first section in said first image;
comparing said first section and said plurality of sections with said second section;
and
matching said first and second images based upon comparing said first section and said plurality of sections with said second section.
28. A method as recited in claim 1, comprising:
identifying an anatomic feature in each of said first and second images;
identifying respective first and second approximate middle positions of said anatomic feature in said first and second images; and
matching said first and second scans using said first and second approximate middle positions.

29. A method as recited in claim 28, comprising:
selecting a first section of said first image correspond to said first approximate middle position;
selecting a second section of said second image correspond to said second approximate middle position;
comparing said first and second sections; and
matching said first and second scans using said first and second sections.
30. A method as recited in claim 29, comprising:
selecting a plurality of sections adjacent to said first section in said first image;
comparing said first section and said plurality of sections with said second section;
and
matching said first and second images based upon comparing said first section and said plurality of sections with said second section.
31. A method as recited in claim 1, comprising:
analyzing registration of said warped image and said second image;
if said registration does not meet predetermined criteria, retrieving image data corresponding to said first image and reconstructing said first image.
32. A method as recited in claim 31, wherein analyzing said registration comprises using histogram analysis.
33. A method as recited in claim 31, comprising:
reconstructing said first image at a different reconstruction starting point;
repeating said matching, warping and subtracting steps using said first image reconstructed at said different reconstruction starting point; and
re-analyzing said registration.
34. A method as recited in claim 33, comprising:
iteratively selecting said different reconstruction starting point.
35. A method for detecting interval change, comprising:
obtaining a first image of a subject;
obtaining a second image of said subject;
matching said first and second images in a scanning direction;
detecting an interval change in matched first and second images.

36. A method as recited in claim 35, where detecting comprises:
nonlinearly warping said first image; and
subtracting a warped first image from said second image.
37. A method as recited in claim 35, comprising:
obtaining a first three-dimensional image as said first image; and
obtaining a second three-dimensional image as said second image.
38. A method as recited in claim 37, comprising:
obtaining a plurality of first section images as said first three-dimensional image;
obtaining a plurality of second section images as said second three-dimensional
image; and
matching said first and second section images along said scanning direction.
39. A method of detecting interval change, comprising:
obtaining a first scan of a subject having a plurality of sections;
obtaining a second scan of said subject having a plurality of sections;
matching three-dimensionally said first and second scans;
matching two-dimensionally corresponding sections of said first and second scans;
and
detecting an interval change between said first and second scans.
40. A method as recited in claim 39, wherein matching three-dimensionally
comprises matching said first and second scans in a scanning direction.
41. A method as recited in claim 39, comprising:
matching two-dimensionally said corresponding sections of said first and second scans
in first and second directions orthogonal to each other; and
matching three-dimensionally said first and second scans in a third direction
orthogonal to each of said first and second directions.
42. A method as recited in claim 41, wherein matching three-dimensionally
comprises matching said first and second scans in a scanning direction.
43. A method as recited in claim 39, wherein matching three-dimensionally
comprises:
identifying an anatomic feature in said first scan;
identifying said anatomic feature in said second scan; and

matching said first and second scans using said anatomic feature.

44. A method as recited in claim 43, comprising:

using said anatomic feature to select a first section of said first scan;

using said anatomic feature to select a second section of said second scan;

comparing said first and second sections; and

matching said first scan with said second scan based upon said comparing step.

45. A method as recited in claim 44, comprising:

selecting a plurality of sections adjacent to said first section in said first scan;

comparing said first section and said plurality of sections with said second section;

and

matching said first scan with said second scan based upon comparing said first section and said plurality of sections with said second section.

46. A method as recited in claim 45, comprising:

matching one of said first section and said plurality of adjacent sections with said second section; and

matching remaining sections of said first scan with remaining sections of said second scan.

47. A computer program product, comprising:

a computer storage medium and a computer program code mechanism embedded in the computer storage medium for processing an image generated in an image processing apparatus, the computer program code mechanism comprising:

a first code device configured to match first and second images of a subject in a scanning direction;

a second code device configured to detect an interval change in matched first and second images.

48. A computer program product as recited in claim 47, comprising:

a third code device configured to match three-dimensionally said first and second images; and

a fourth code device configured to match two-dimensionally corresponding sections of said first and second images.

49. A computer program product as recited in claim 47, comprising:

a third code device configured to identify an anatomic feature in said first image;
a fourth code device configured to identify said anatomic feature in said second image; and
said second code device configured to match said first and second images using said anatomic feature.

50. A computer program product as recited in claim 49, comprising:
a fifth code device configured to determine a first relative area of said anatomic feature in said first image;
a sixth code device configured to determine a second relative area of said anatomic feature in said second image;
a seventh code device configured to select a first portion of said first image using said first relative area; and
an eighth code device configured to select a second portion of said second image using said second relative area.

51. A computer program product as recited in claim 50, comprising:
a ninth code device configured to determine a first average and a second average of said first and second relative areas, respectively;
a tenth code device configured to select one section of said first image corresponding to said first average; and
an eleventh code device configured to select one section of said second image corresponding to said second average.

52. A computer program product as recited in claim 51, comprising:
said tenth code device configured to select said one section of said first image and a number of adjacent sections of said first image as comparison sections; and
a twelfth code device configured to compare each section of said comparison sections to said one section of said second image.

53. A computer program product as recited in claim 49, comprising:
a fourth code device configured to use said anatomic feature to select a first section of said first image;
a fifth code device configured to use said anatomic feature to select a second section of said second image;

a sixth code device configured to compare said first and second sections; and
said second code device configured to match said first image with said second image based upon said comparing step.

54. A computer program product as recited in claim 53, comprising:

a seventh code device configured to select a plurality of sections adjacent to said first section in said first image;

said sixth code device configured to compare said first section and said plurality of sections with said second section; and

said second code device configured to match said first image with said second image based upon comparing said first section and said plurality of sections with said second section.

55. A computer program product as recited in claim 54, comprising:

said second code device configured to match one of said first section and said plurality of adjacent sections with said second section; and

said second code device configured to match remaining sections of said first image with remaining sections of said second image.

56. A computer program product as recited in claim 47, comprising:

a third code device configured to nonlinearly warp said first image; and

a fourth code device configured to subtract a warped first image from said second image.

57. An interval change detecting system, comprising:

one of a three-dimensional image acquisition device and a three-dimensional image storage device;

a scanning direction image matching device connected to one of said image acquisition device and said image storage device;

an image subtraction device connected to said matching device.

58. A system as recited in claim 57, comprising:

said image having a plurality of sections; and

a two-dimensional image matching device connected to one of said image acquisition device and said image storage device.

59. A system as recited in claim 57, comprising:

a relative area determination circuit connected to one of said image acquisition device and said image storage device; and

a two-dimensional image matching circuit connected to said relative area determination circuit.

60. A system as recited in claim 59, comprising:

a local matching circuit connected to said two-dimensional matching circuit.

61. A system as recited in claim 60, comprising:

a warping circuit connected to said local matching circuit.

62. A system as recited in claim 60, wherein said local matching circuit comprises a cross-correlation circuit.

63. A system as recited in claim 57, comprising:

a registration analysis circuit connected to said subtraction circuit.

64. A system as recited in claim 63, wherein said registration analysis circuit comprises:

a histogram analysis circuit;

an image data retrieval circuit connected to said histogram analysis circuit; and

an image reconstruction circuit connected to said image data retrieval circuit.

1/21

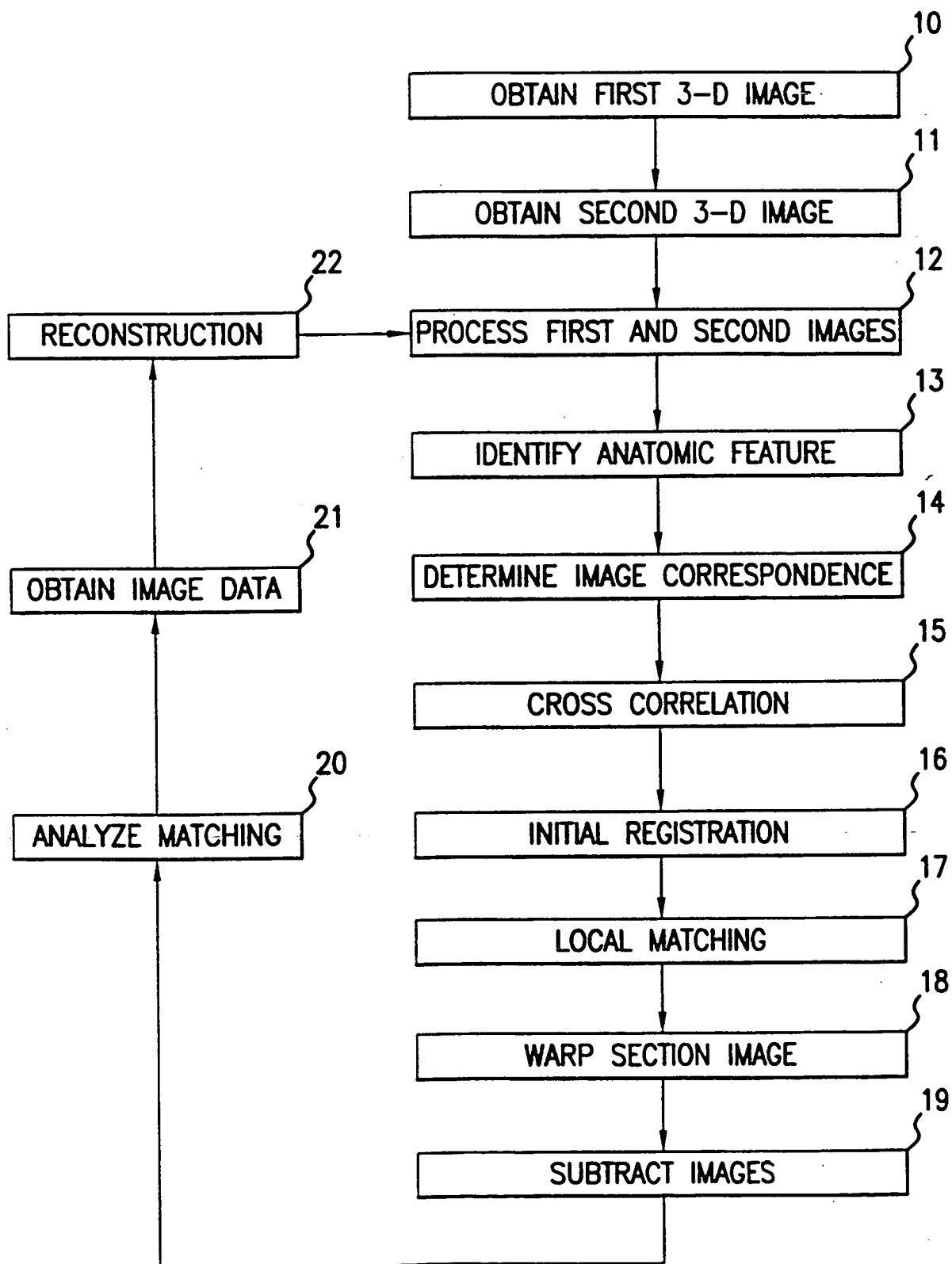


FIG.1

2/21

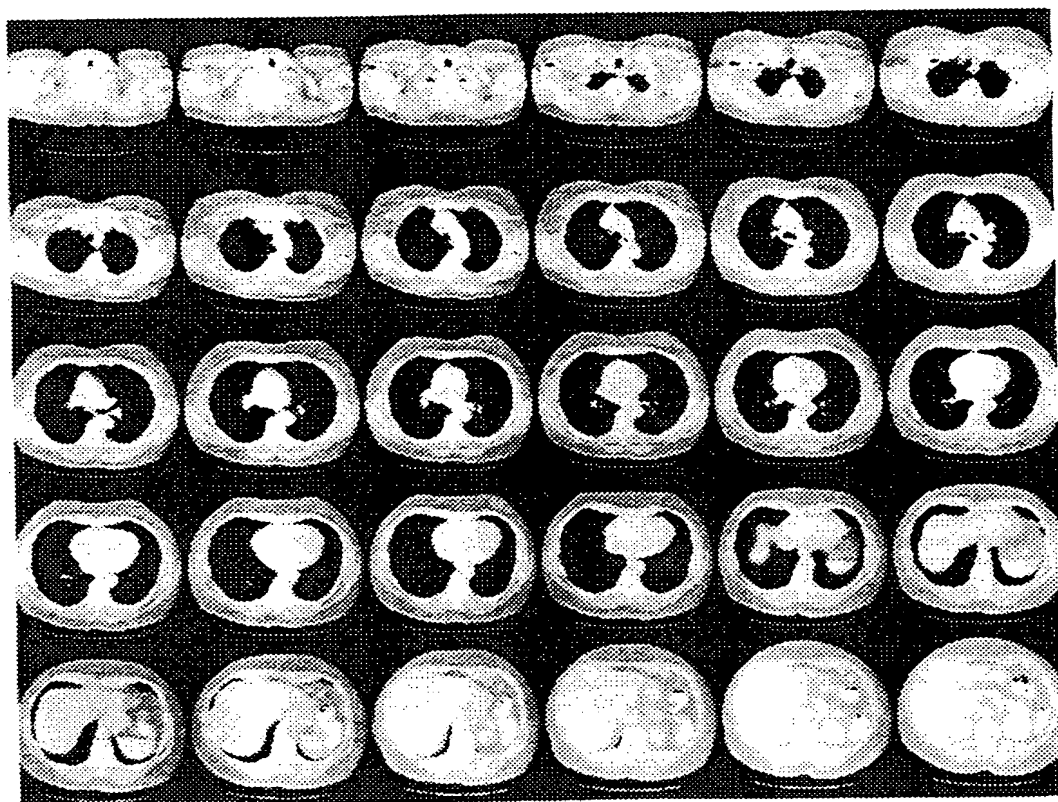


FIG.2A

3/21

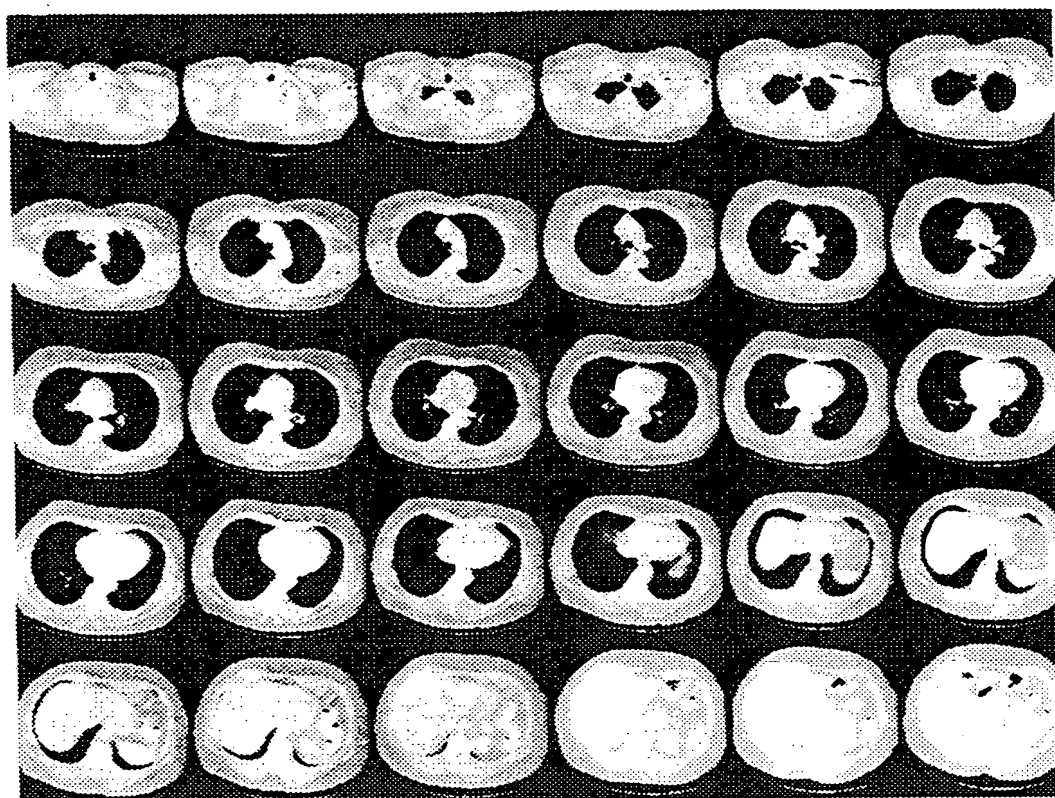


FIG.2B

4/21

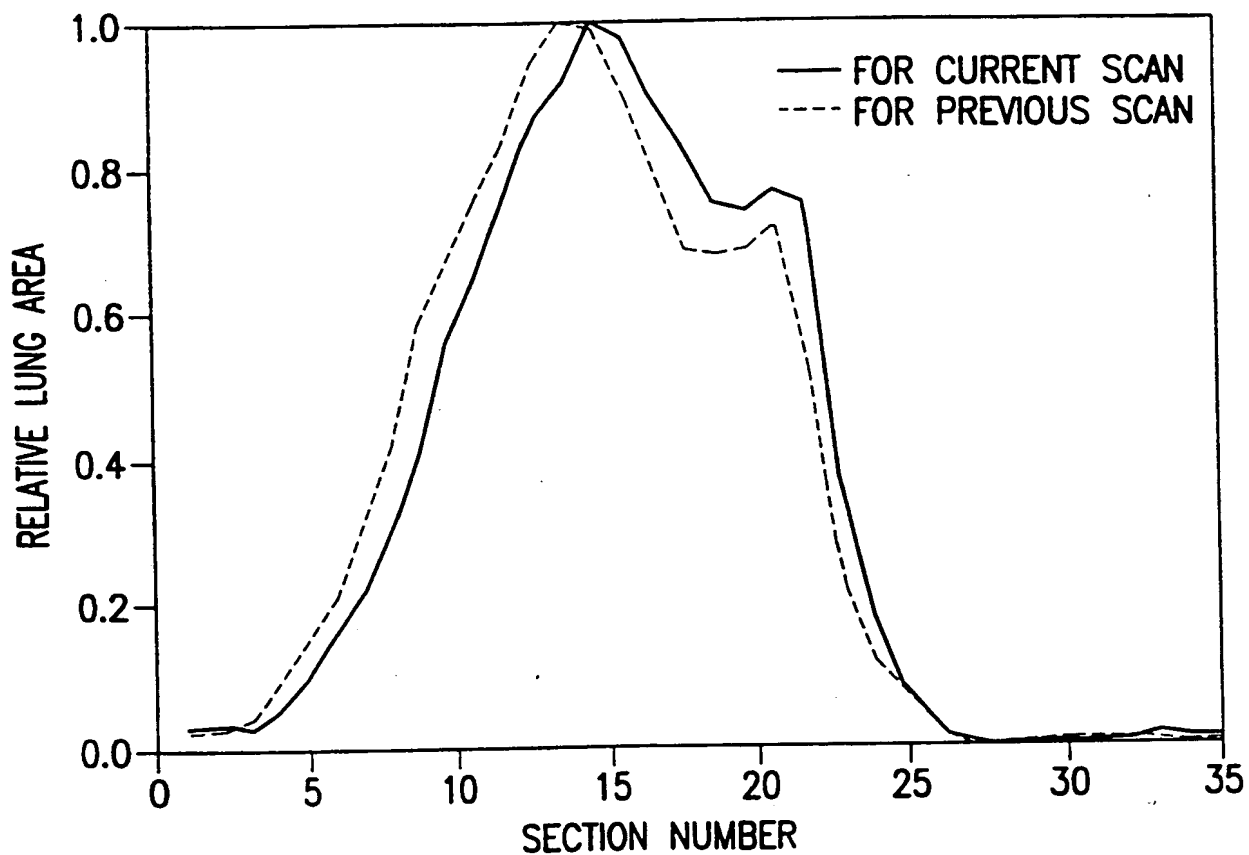


FIG.3

5/21

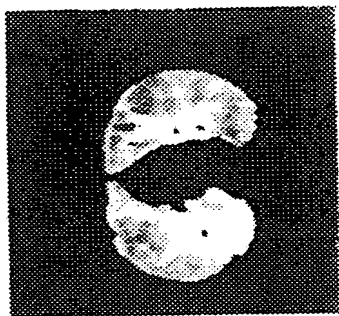


FIG. 4A

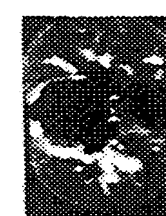


FIG. 4B FIG. 4C FIG. 4D FIG. 4E FIG. 4F

6/21

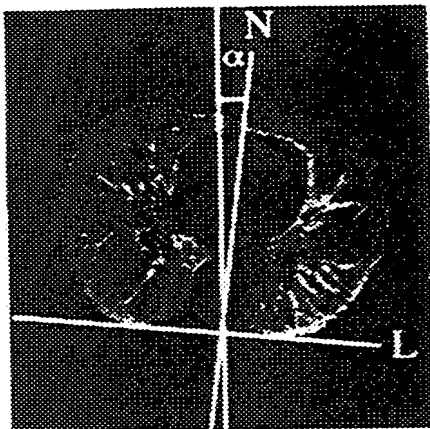


FIG. 5A

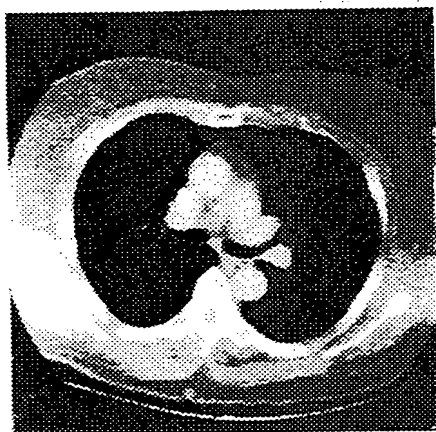


FIG. 5B

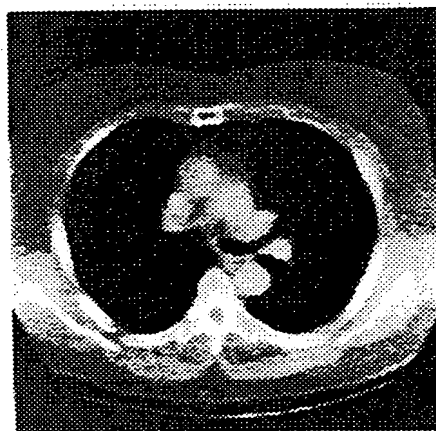


FIG. 5C

7/21

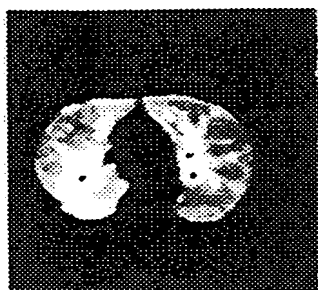


FIG. 6A



FIG. 6B

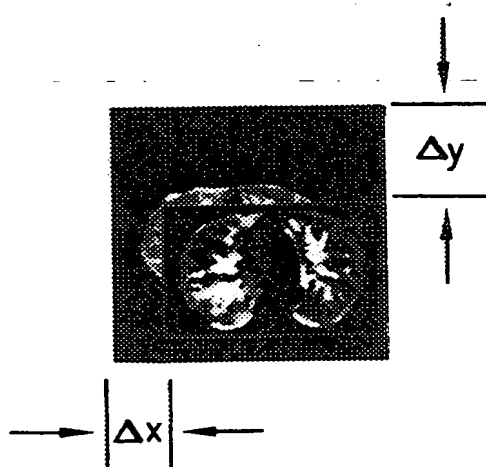


FIG. 6C

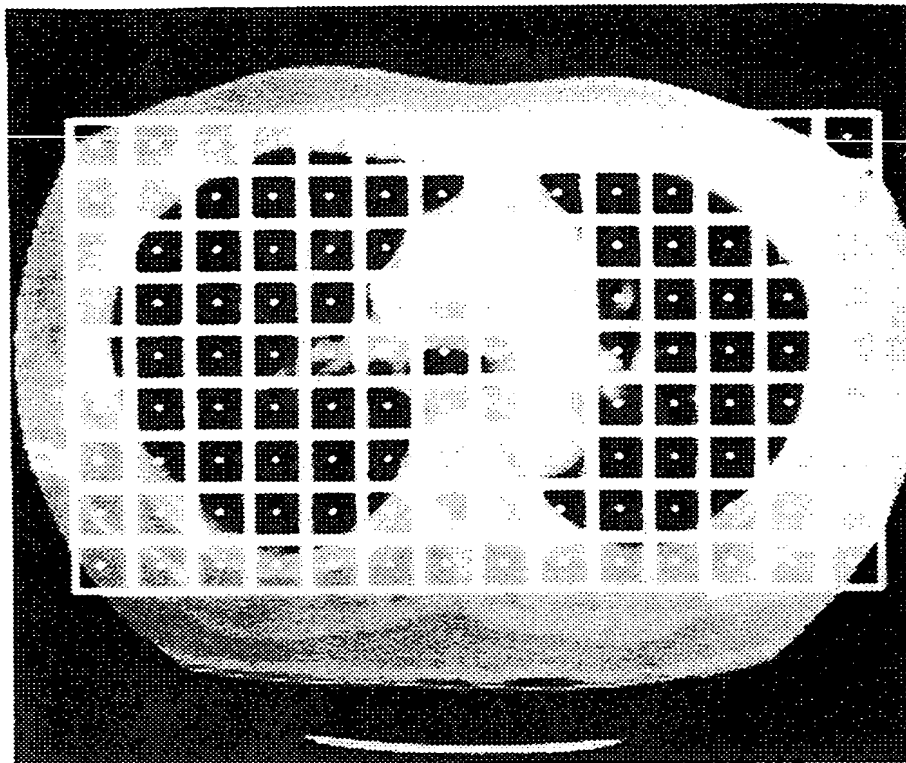


FIG. 7A

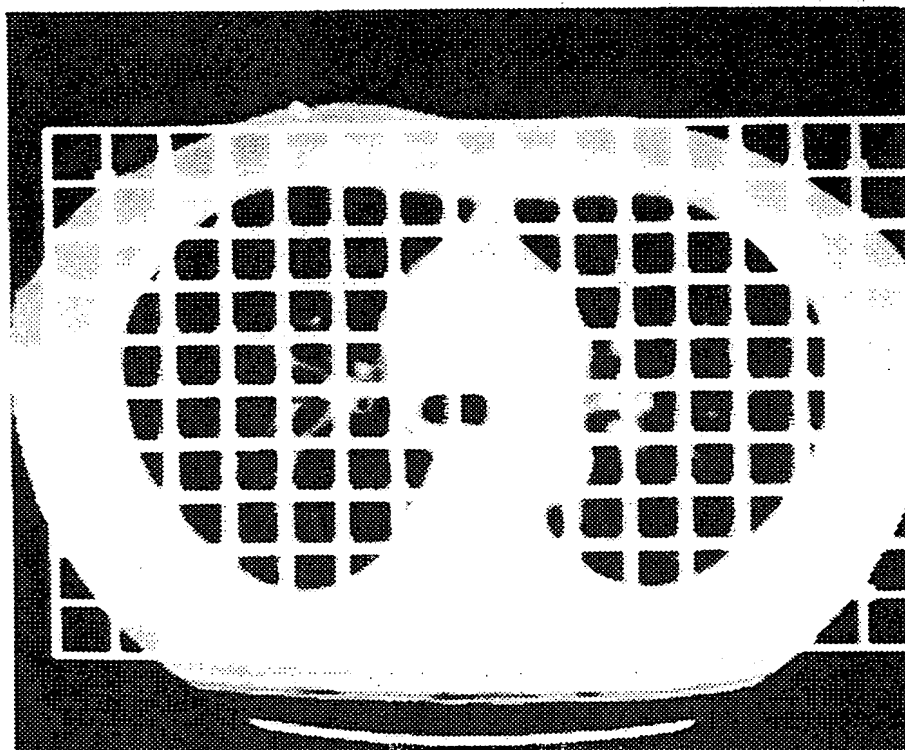


FIG. 7B

SUBSTITUTE SHEET (RULE 26)

9/21

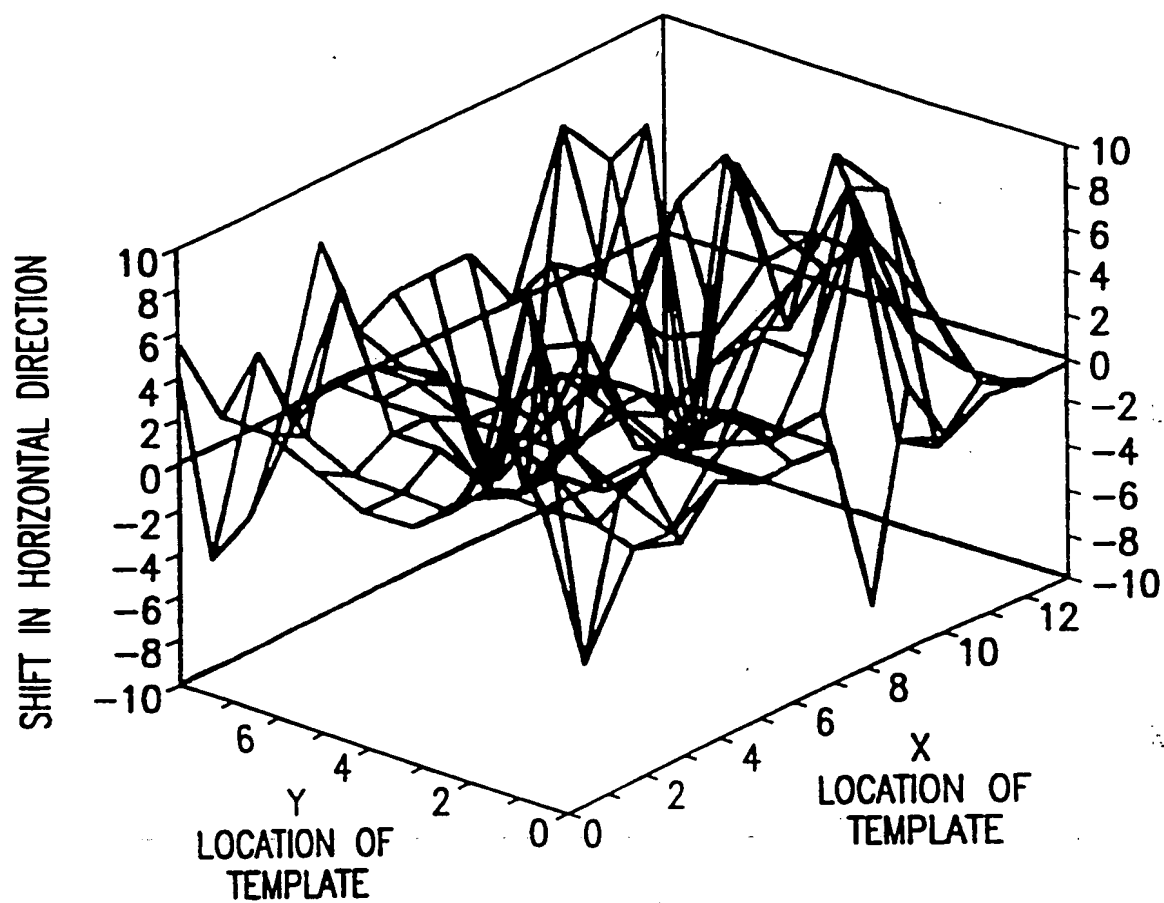


FIG.8A

10 / 21

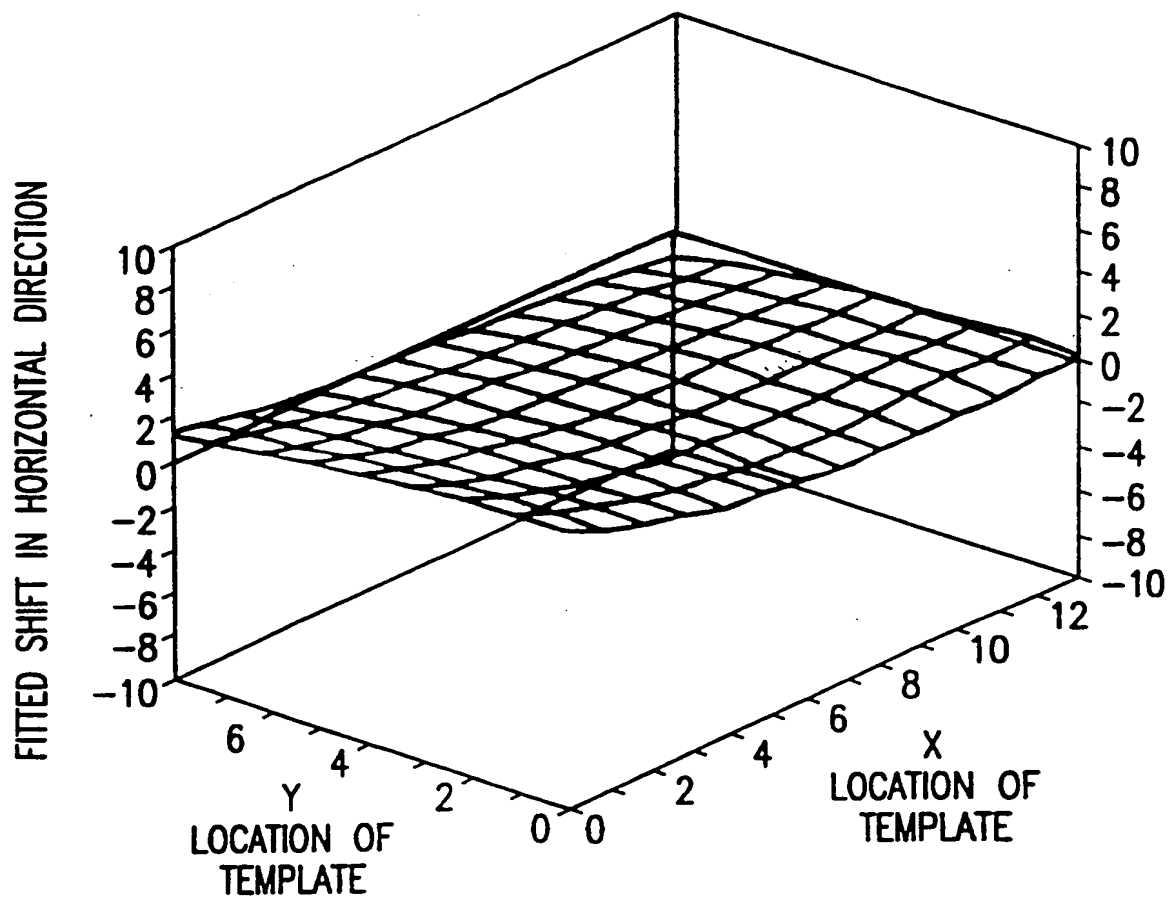


FIG.8B

11/21

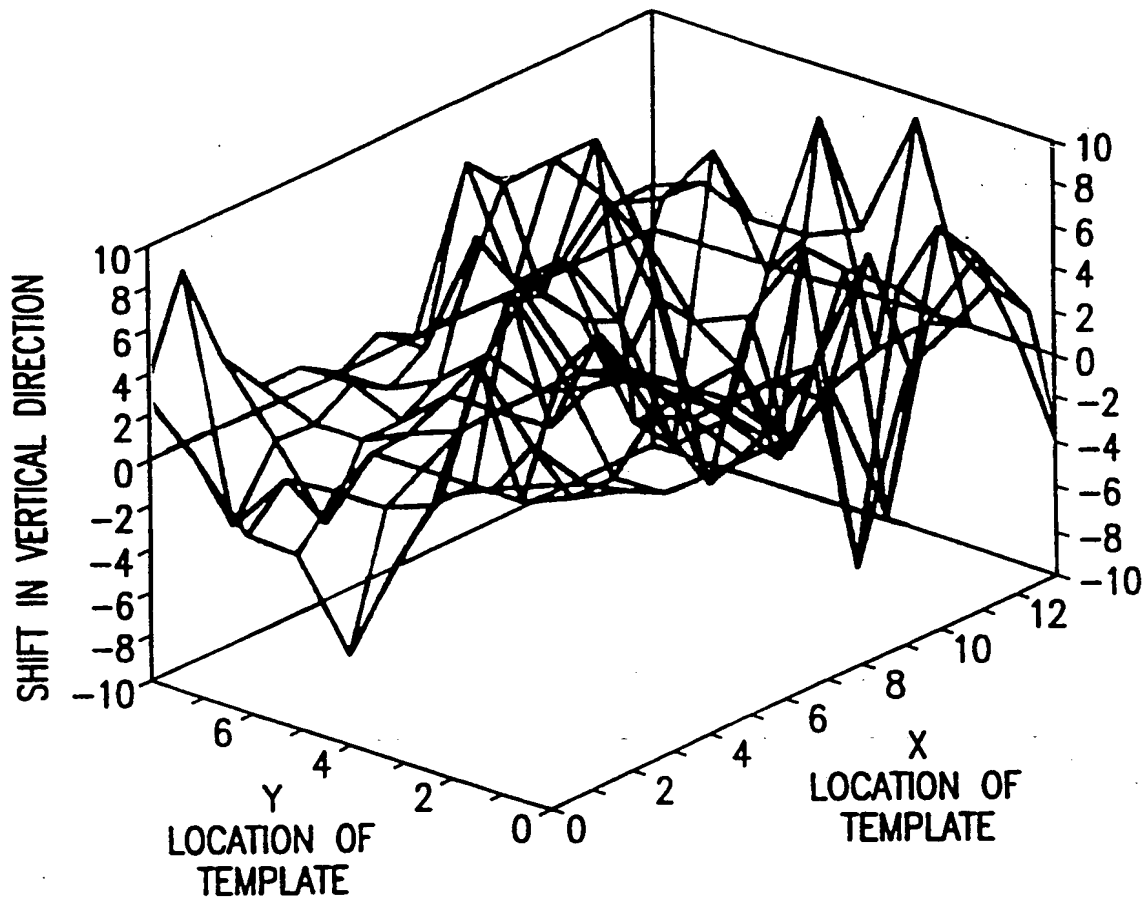


FIG.9A

12/21

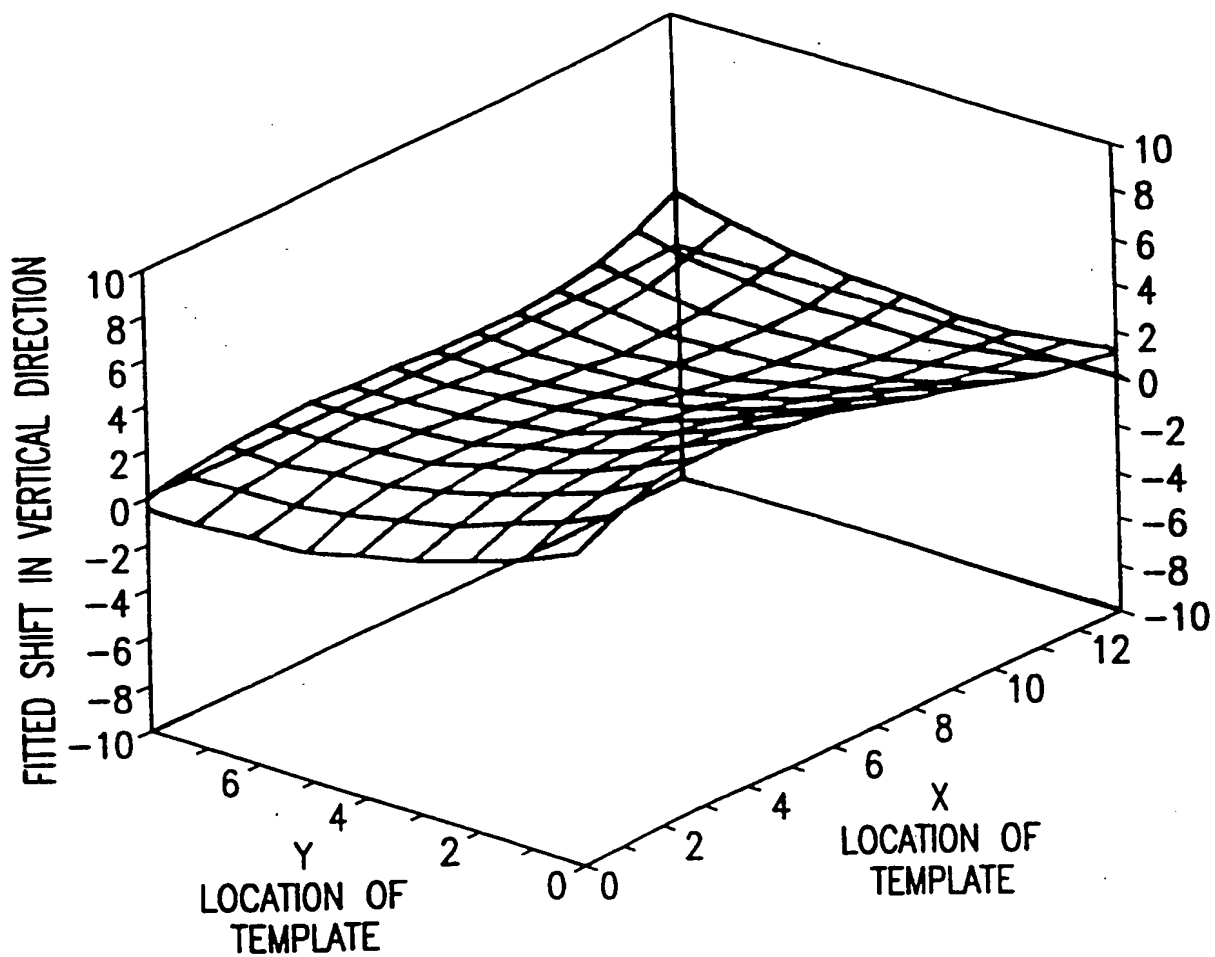


FIG.9B

13/21

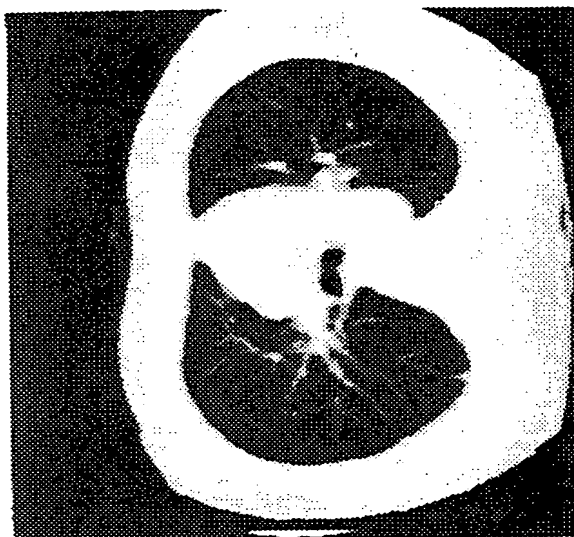


FIG.10B

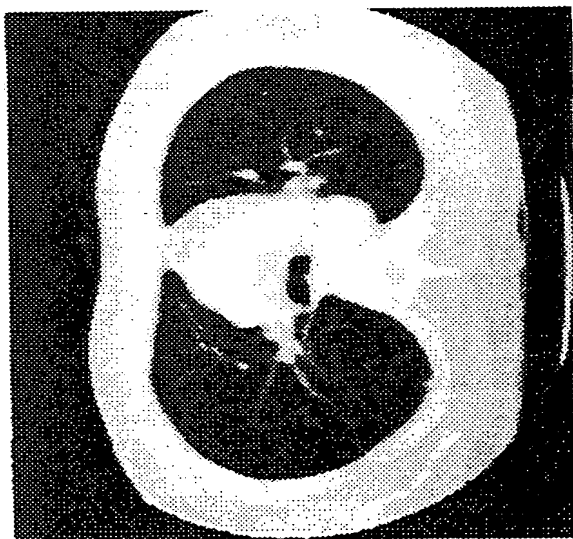


FIG.10A

14/21

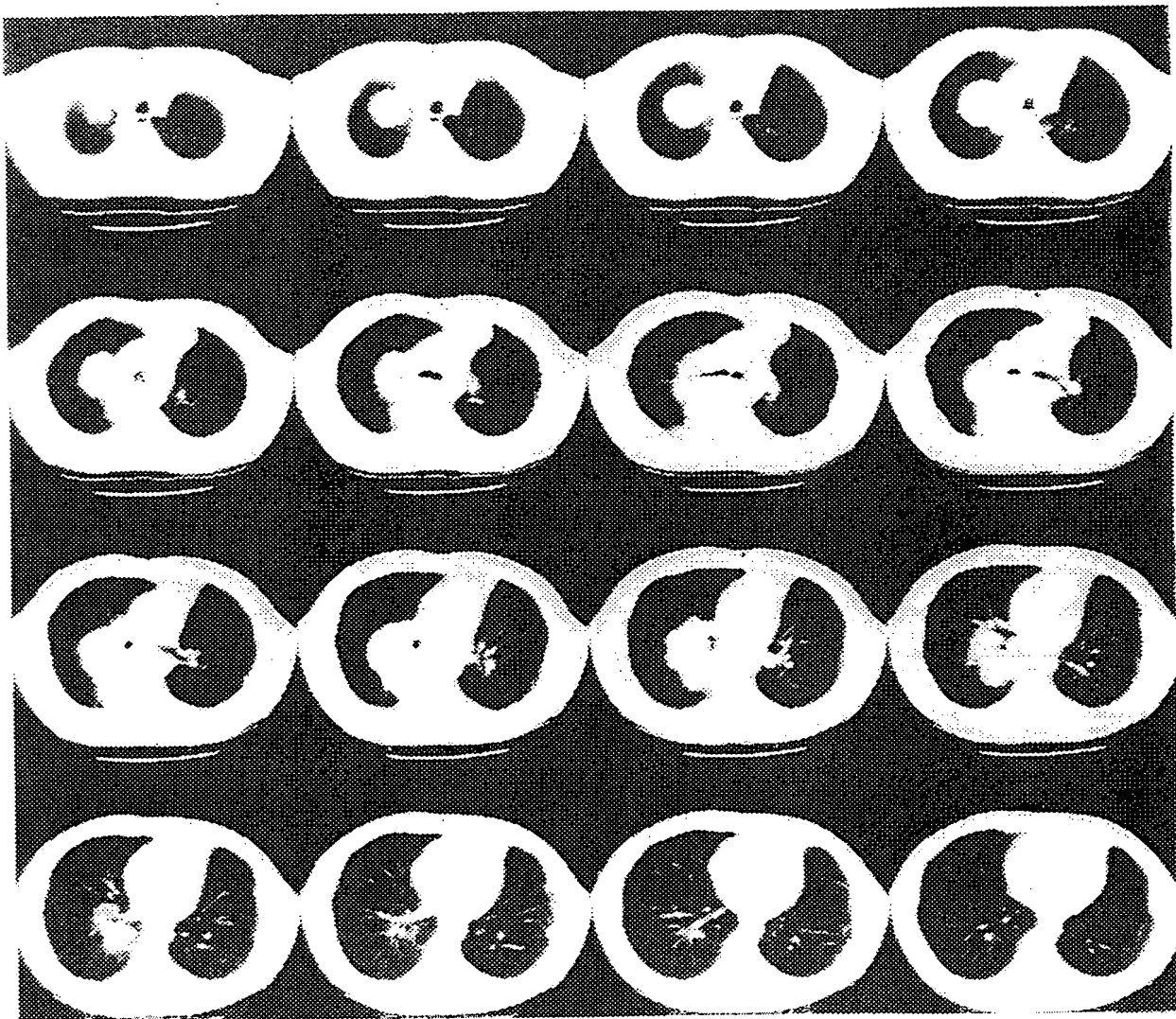


FIG.11A

15/21

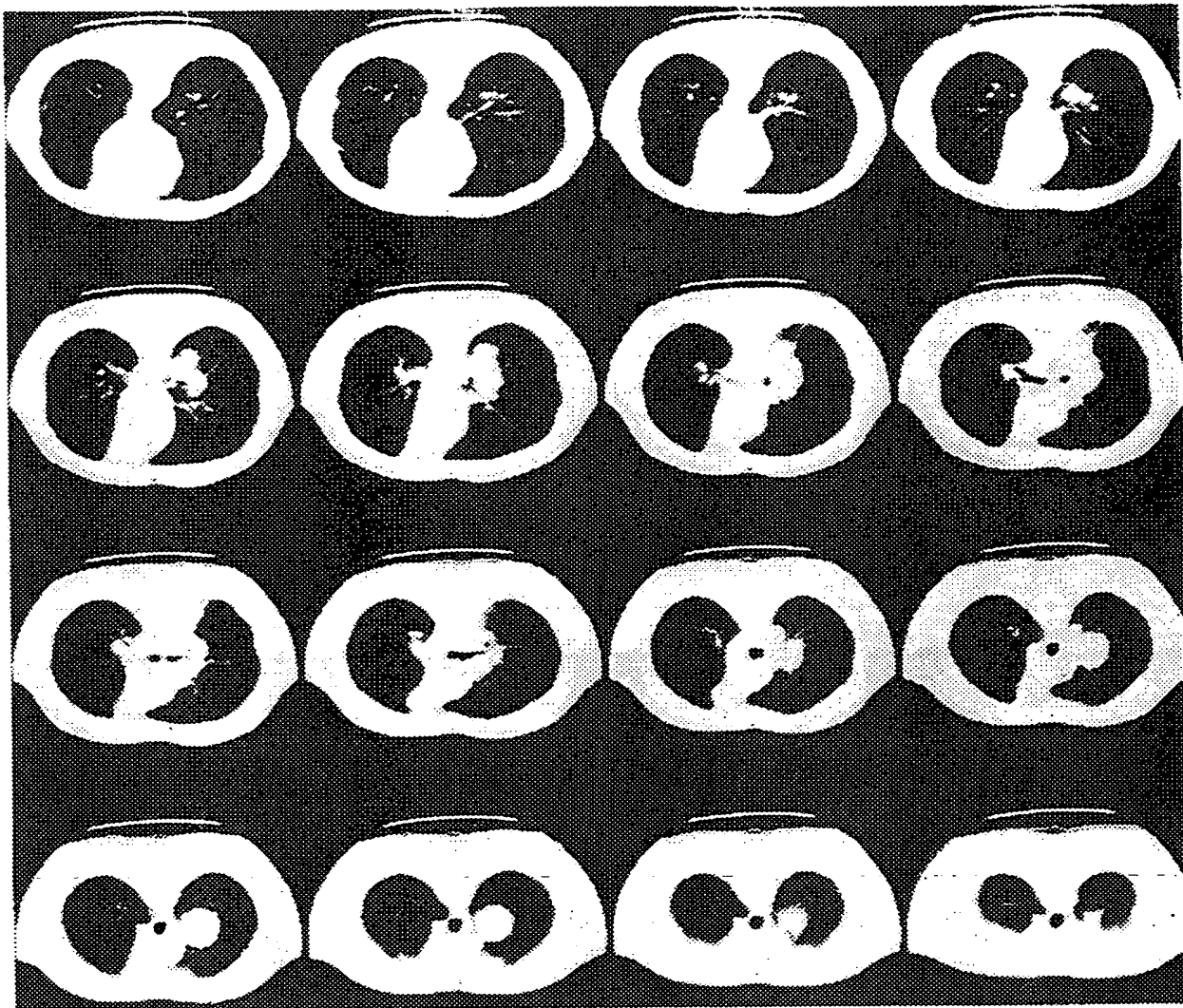


FIG. 11B

16/21

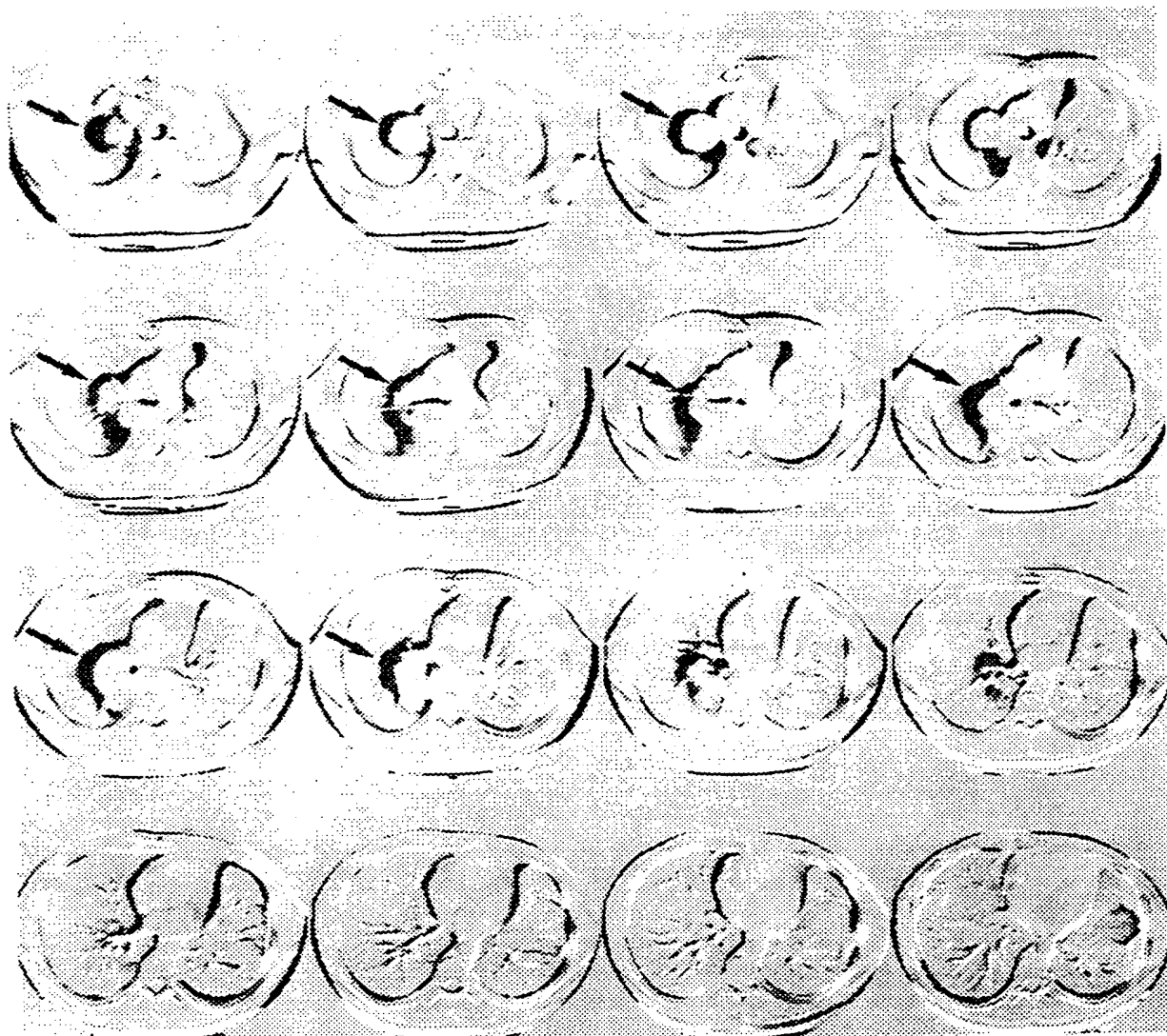


FIG.11C

17/21

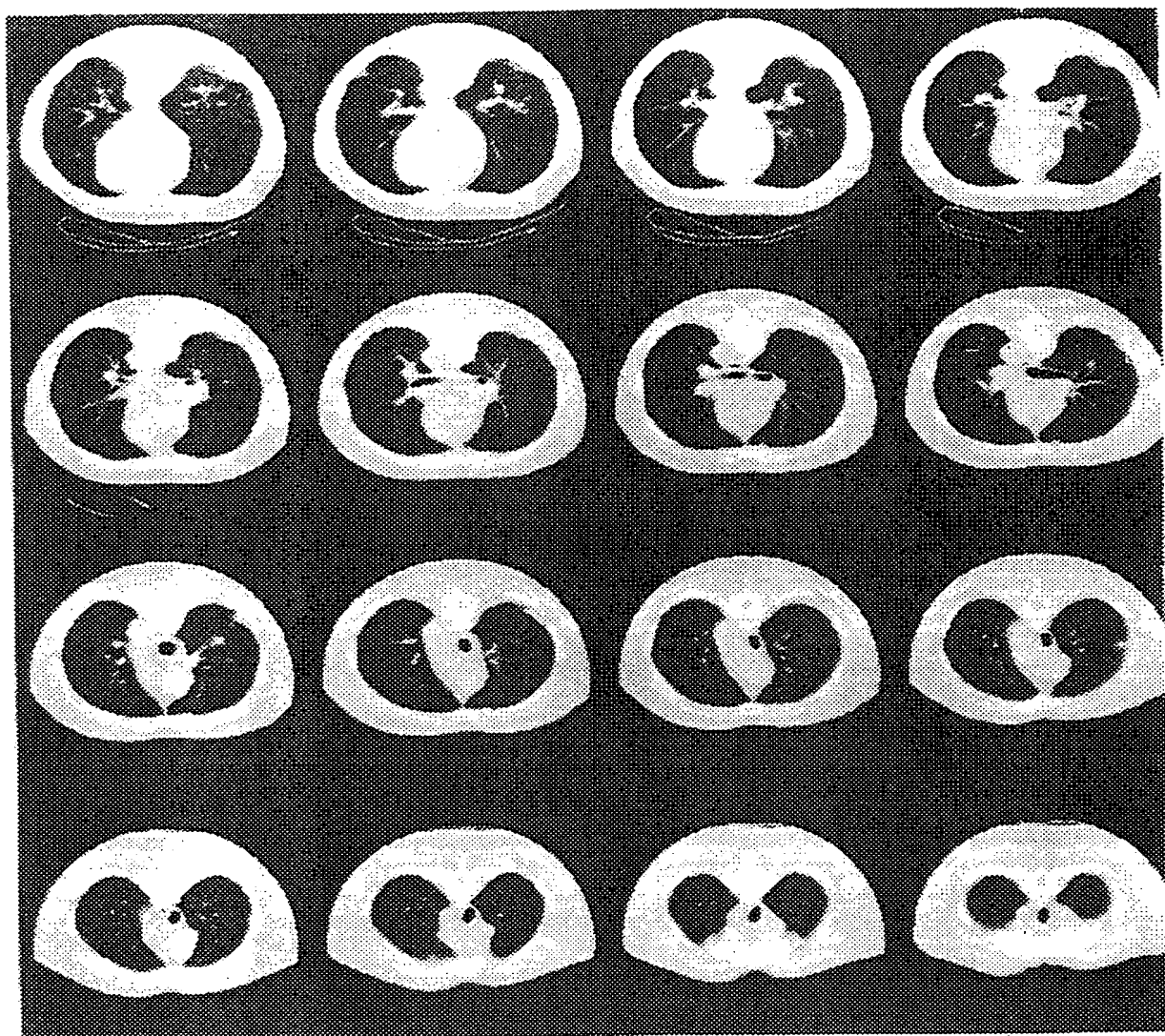


FIG. 12A

18/21

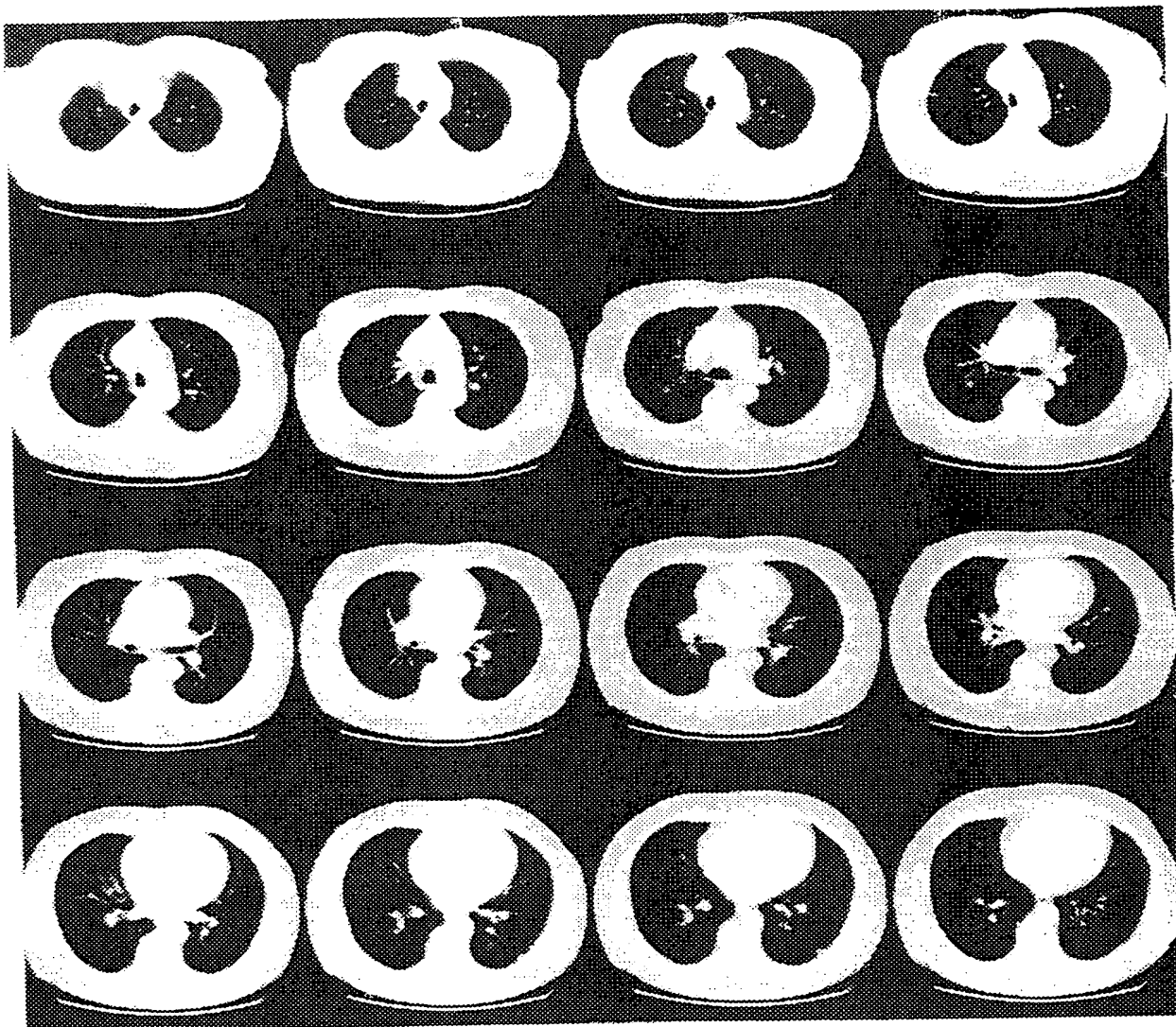


FIG.12B

19/21

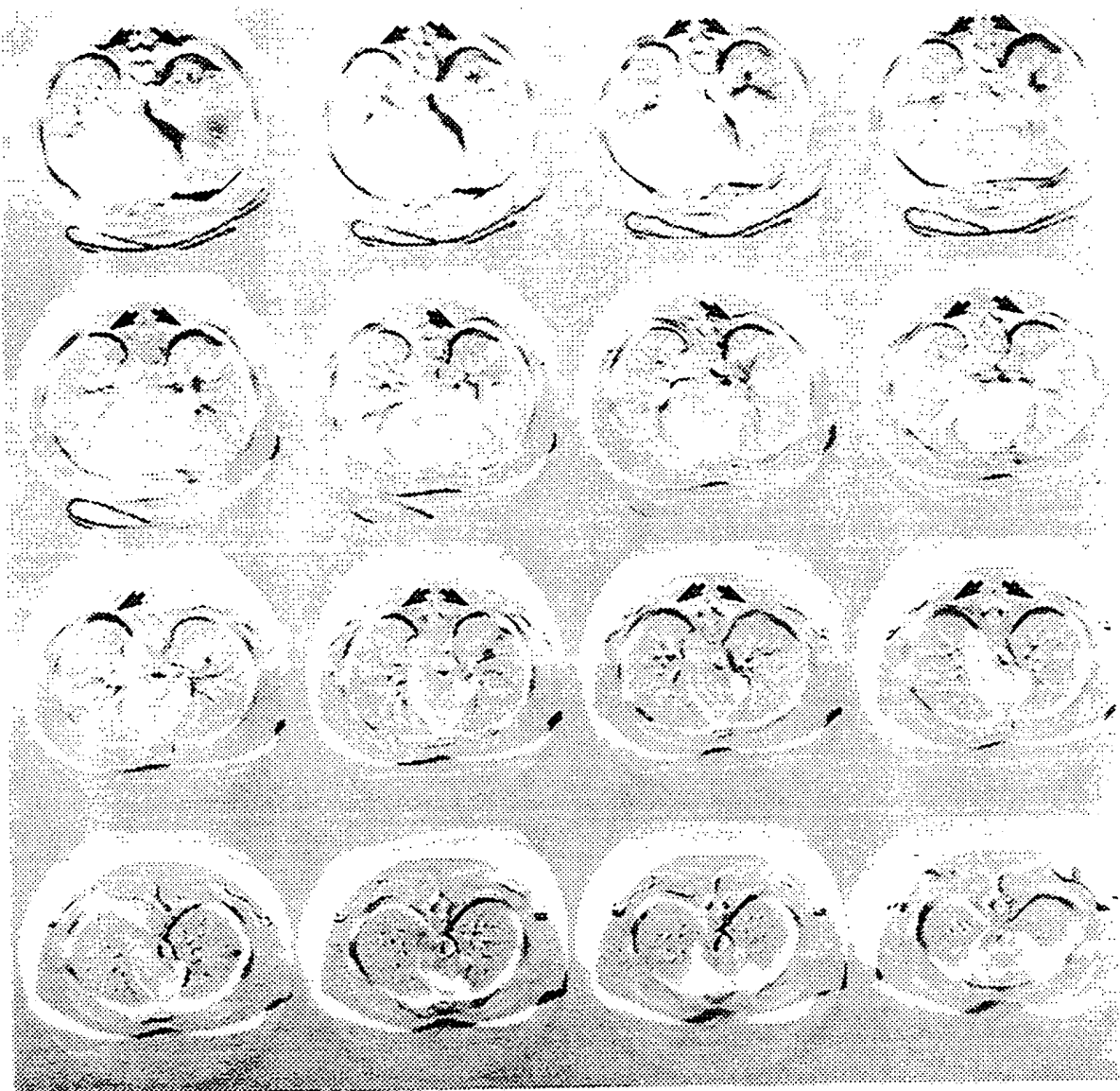


FIG.12C

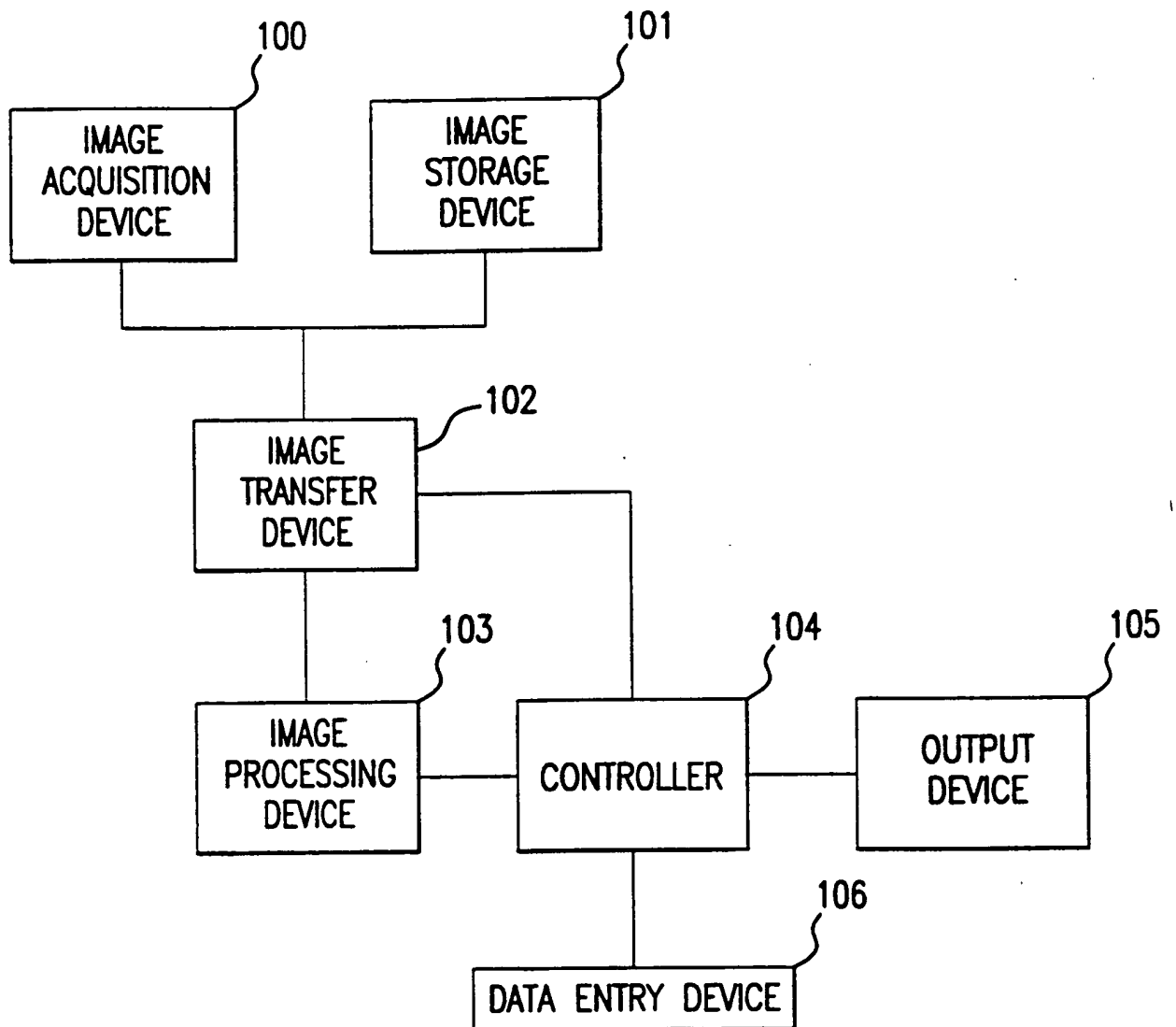


FIG.13

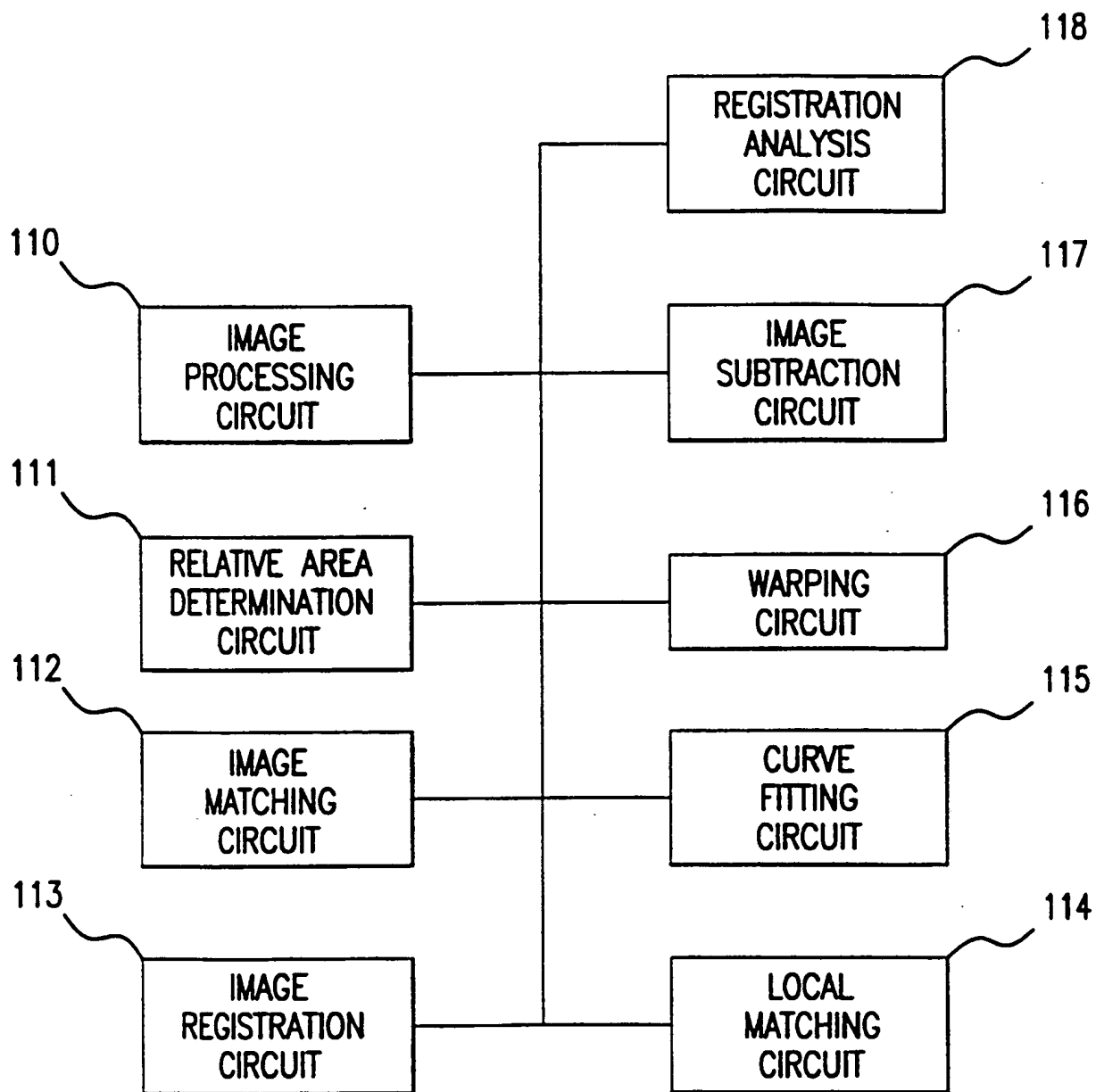


FIG.14

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US99/03282

A. CLASSIFICATION OF SUBJECT MATTER

IPC(G) : G06K 9/00

US CL : 382/128, 131, 294; 128/922; 378/901; 250/363.04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 382/128, 131, 294; 128/922; 378/901; 250/363.04

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS, CAS ONLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,633,951 A (MOSHFEGHI) 27 MAY 1997, col. 2 line 23-col. 3 line 37	1-3, 18-20, 31-34, 39- 44, 57-59
-----		-----
Y		4-17, 21-30 35-38, 45-56, 60-64
Y	US 5,359,513 A (KANO et al.) 25 OCTOBER 1994, Figs 1b-1d col. 2 line 3-col. 3 line 29	4-17, 21-30, 35-38, 45-56, 60-64
Y	US 5,881,124 A (GIGER et al.) 09 MARCH 1999, Fig. 23 col. 2 lines 2-39	4-17, 21-30, 35-38, 45-56, 60-64
Y	US 5,319,549 A (KATSURAGAWA et al.) 07 JUNE 1994, Fig. 2A col. 2 line 12-col. 3 line 10	6-17, 35-38, 45-56, 60-64

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
A document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
E earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*G* document member of the same patent family
O document referring to an oral disclosure, use, exhibition or other means	
P document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

15 APRIL 1999

Date of mailing of the international search report

06 MAY 1999

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

JINGGE WU

Telephone No. (703) 305-3900

1/15

107

FIG. 1

OBTAIN FIRST 3-D IMAGE

117

OBTAIN SECOND 3-D IMAGE

227

RECONSTRUCTION

127

PROCESS FIRST AND SECOND IMAGES

137

IDENTIFY ANATOMIC FEATURE

217

OBTAIN IMAGE DATA

147

DETERMINE IMAGE CORRESPONDENCE

157

CROSS CORRELATION

207

ANALYZE MATCHING

167

INITIAL REGISTRATION

177

LOCAL MATCHING

187

WARP SECTION IMAGE

197

SUBTRACT IMAGES

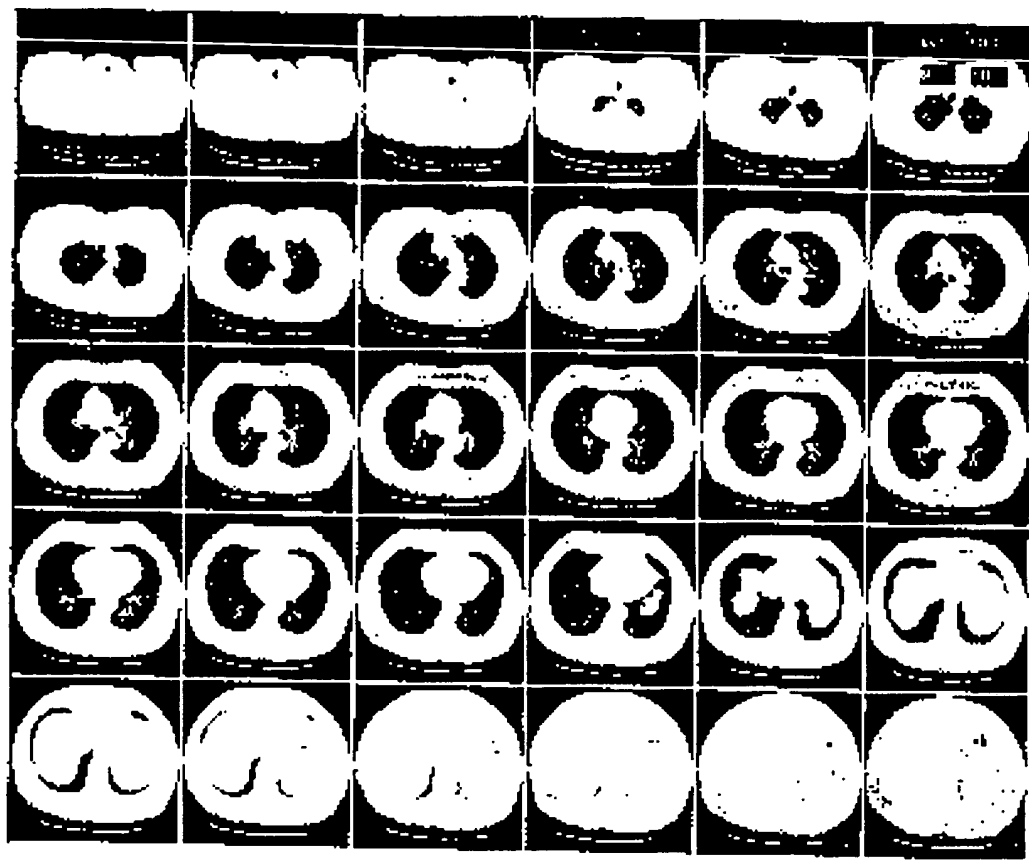


FIG. 2A

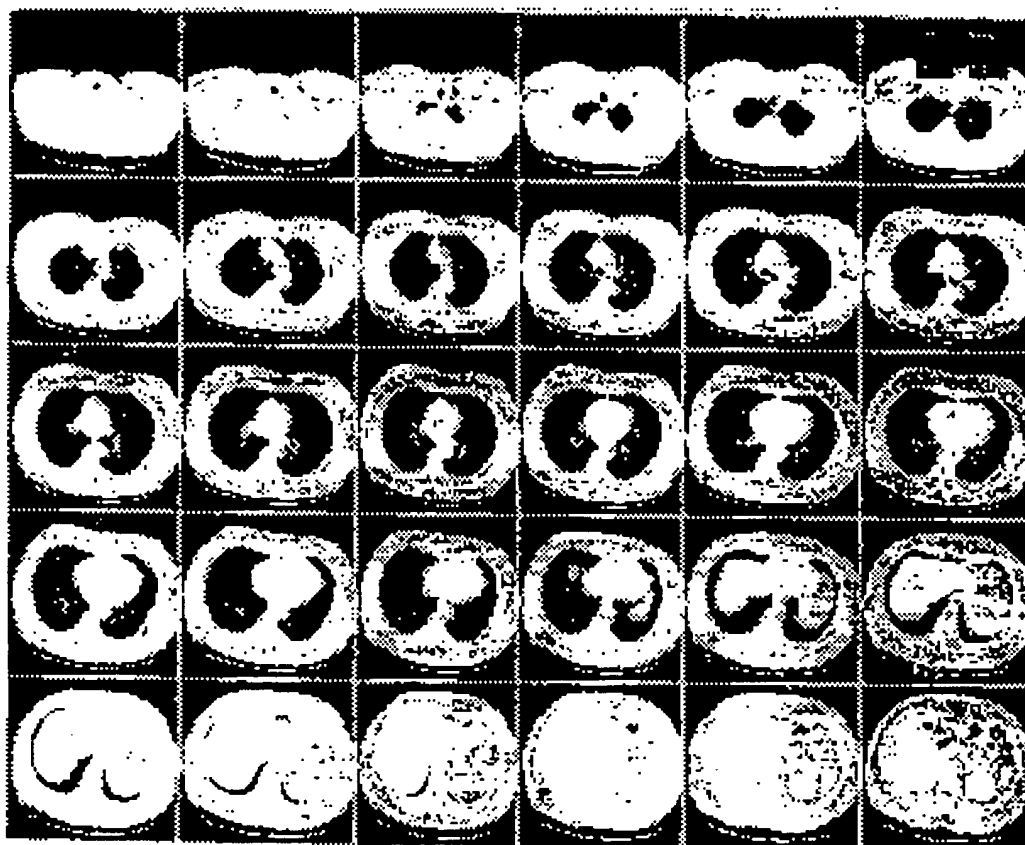


FIG. 2B

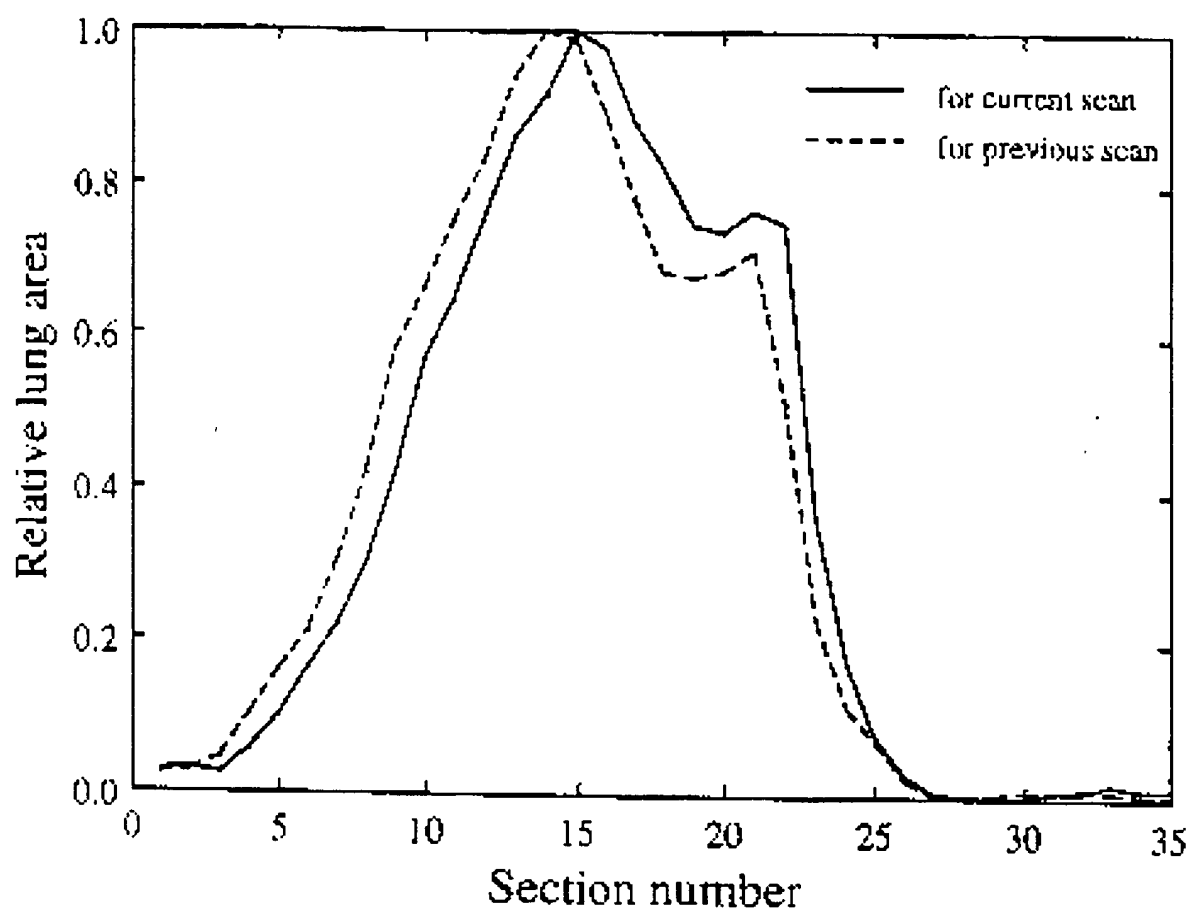


FIG. 3

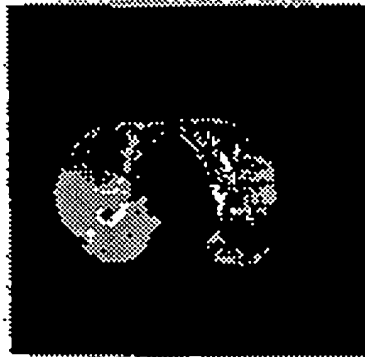


FIG. 4A



FIG. 4B

FIG. 4C

FIG. 4D

FIG. 4E

FIG. 4F

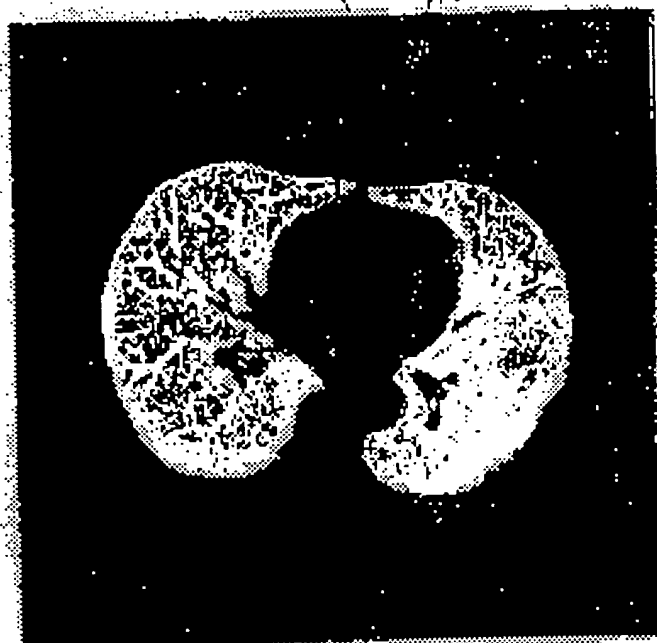


FIG. 5A

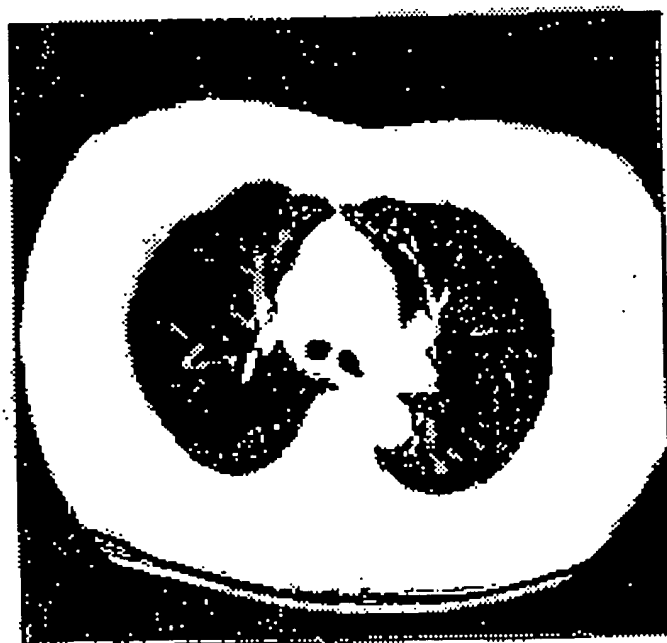


FIG. 5B



FIG. 5C



FIG. 6B



FIG. 6A

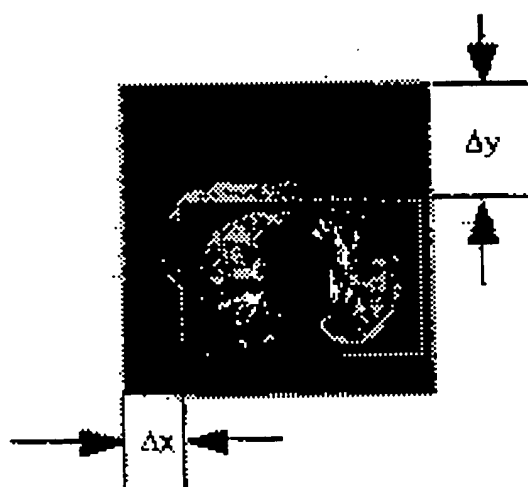


FIG. 6C

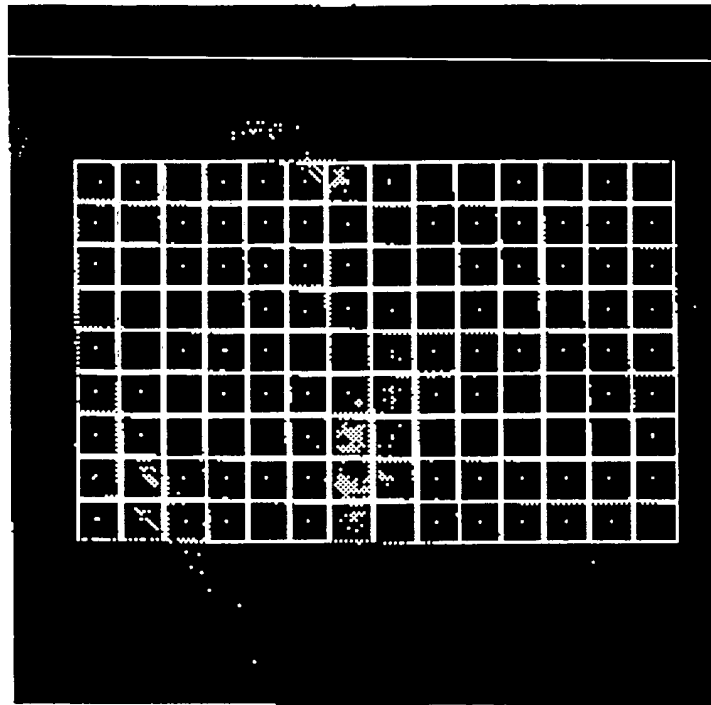


FIG. 7A

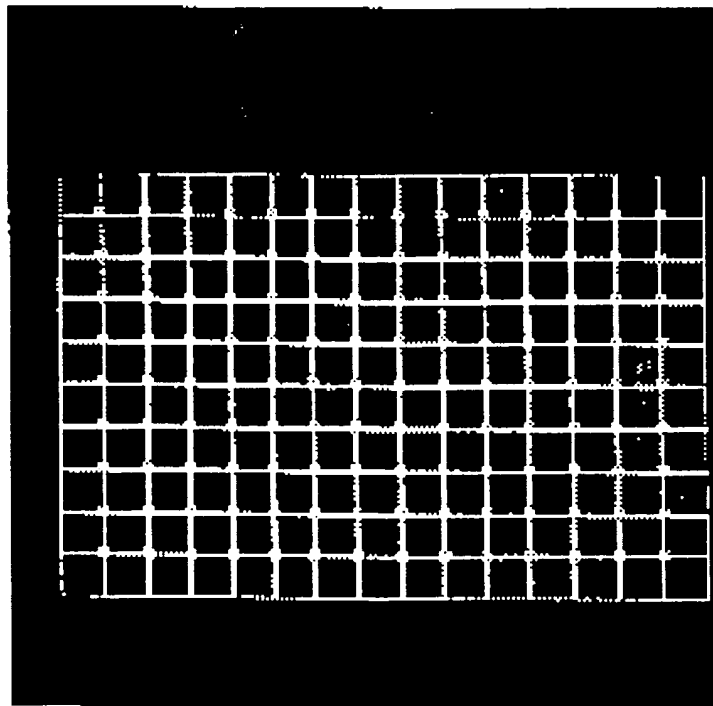


FIG. 7B

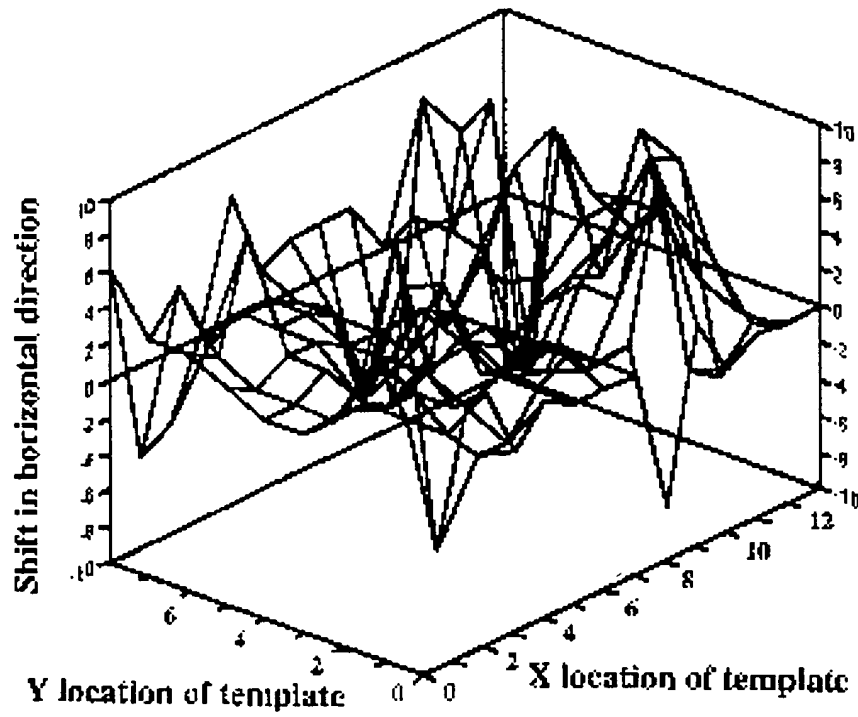


FIG. 8A

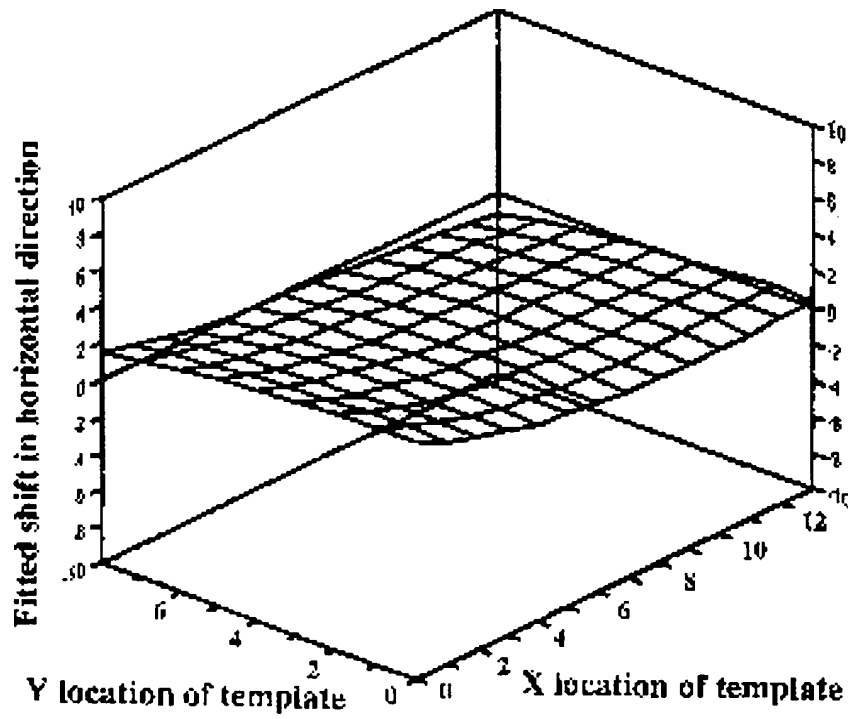


FIG. 8B

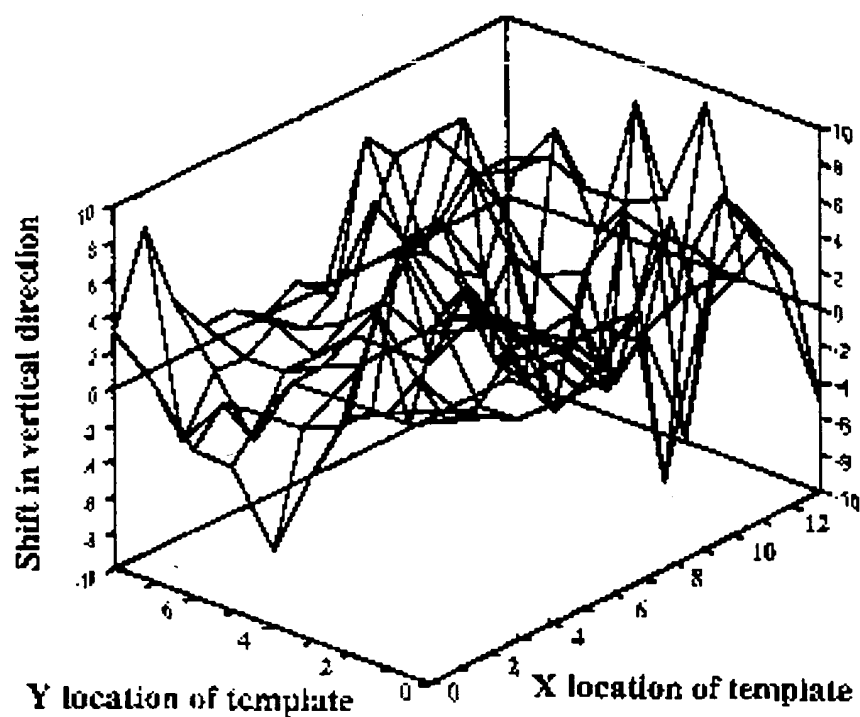


FIG. 9A

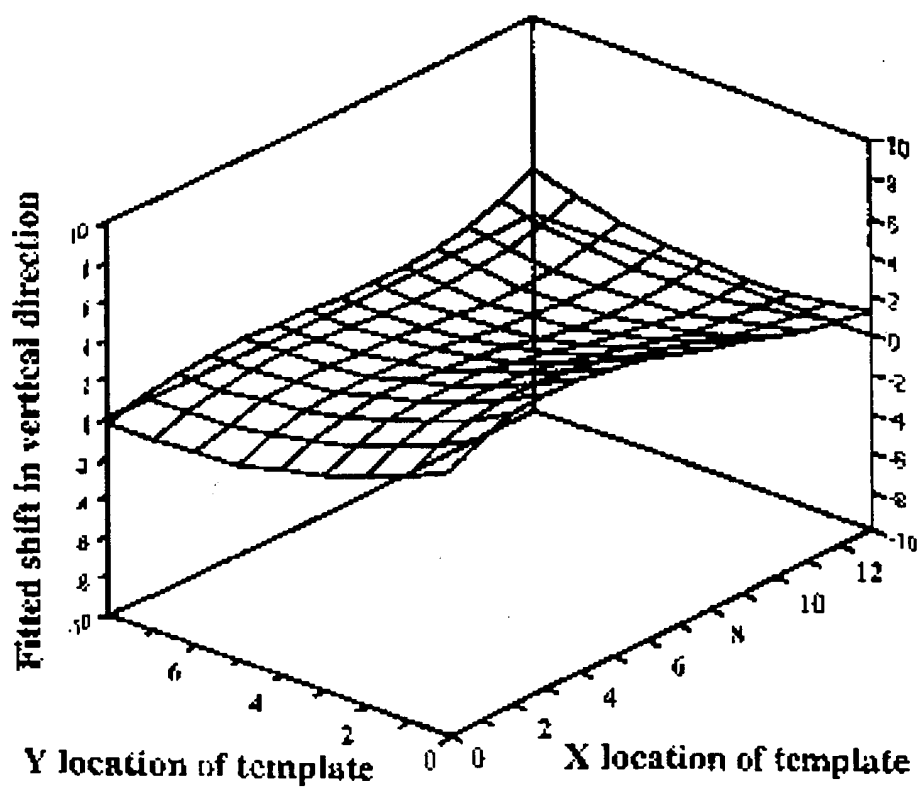


FIG. 9B



FIG. 10A



FIG. 10B

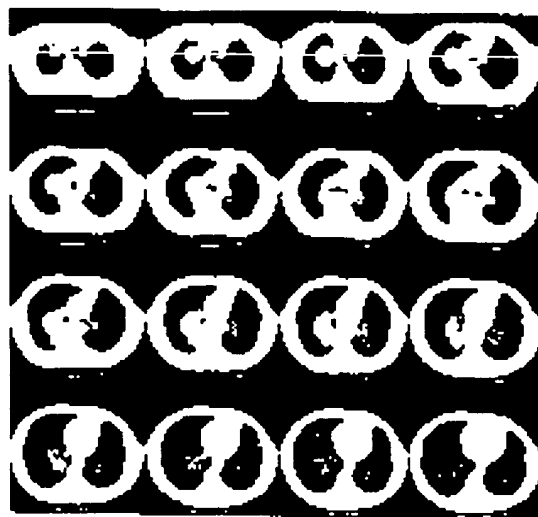


FIG. 11A

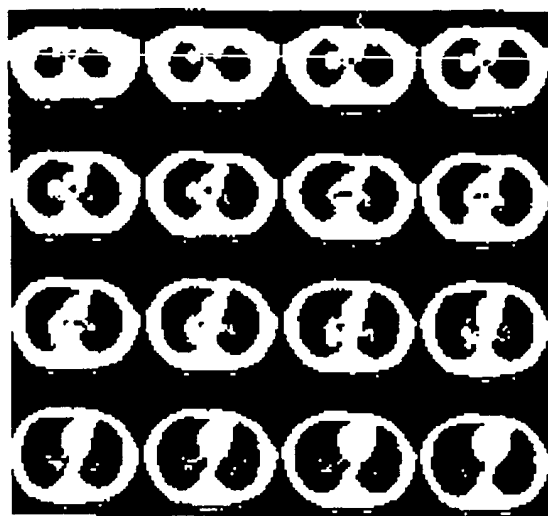


FIG. 11B

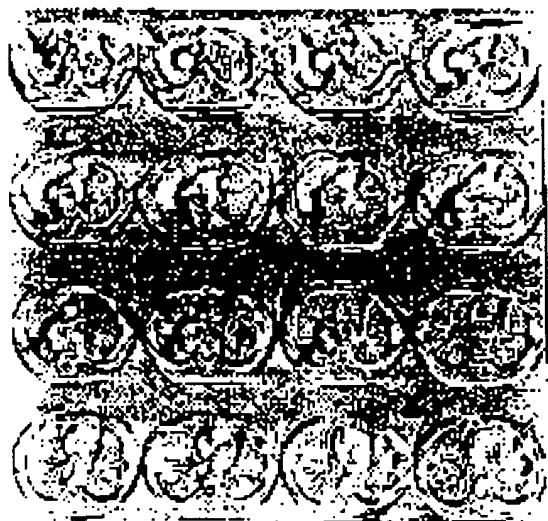


FIG. 11C

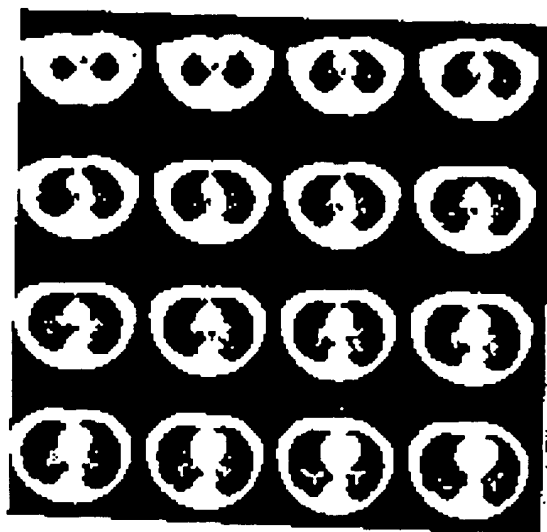


FIG. 12A

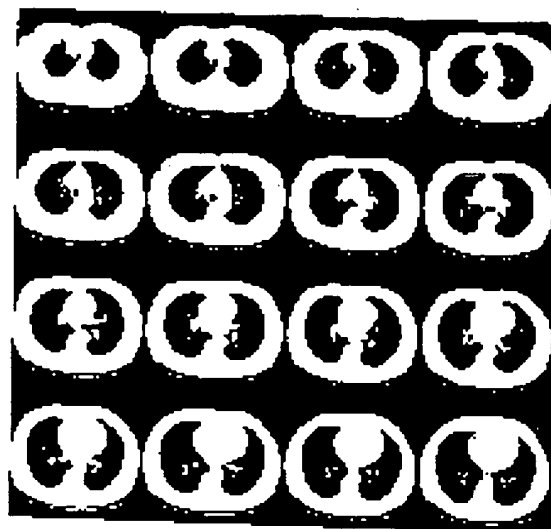


FIG. 12B



FIG. 12C

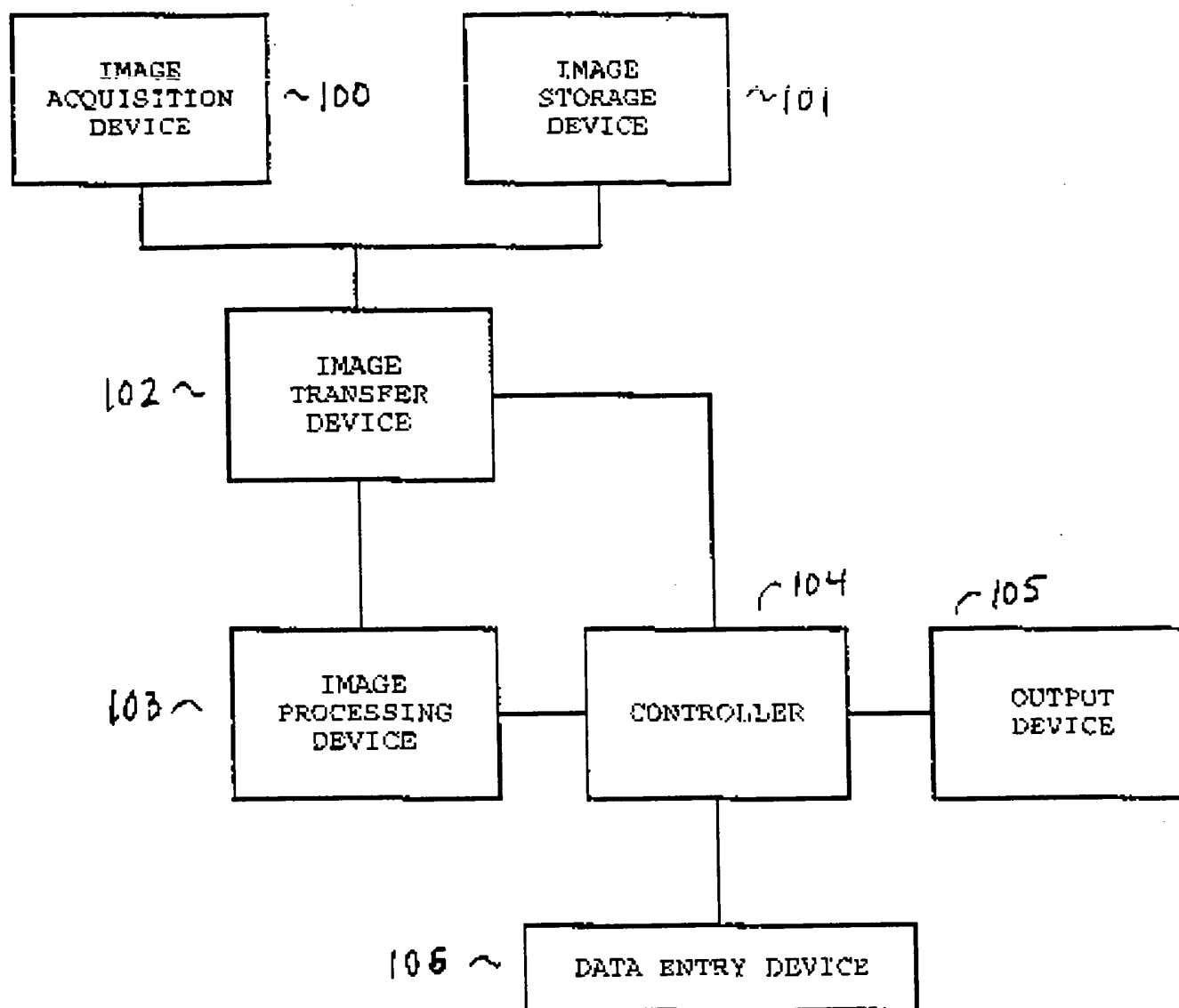


FIG. 13

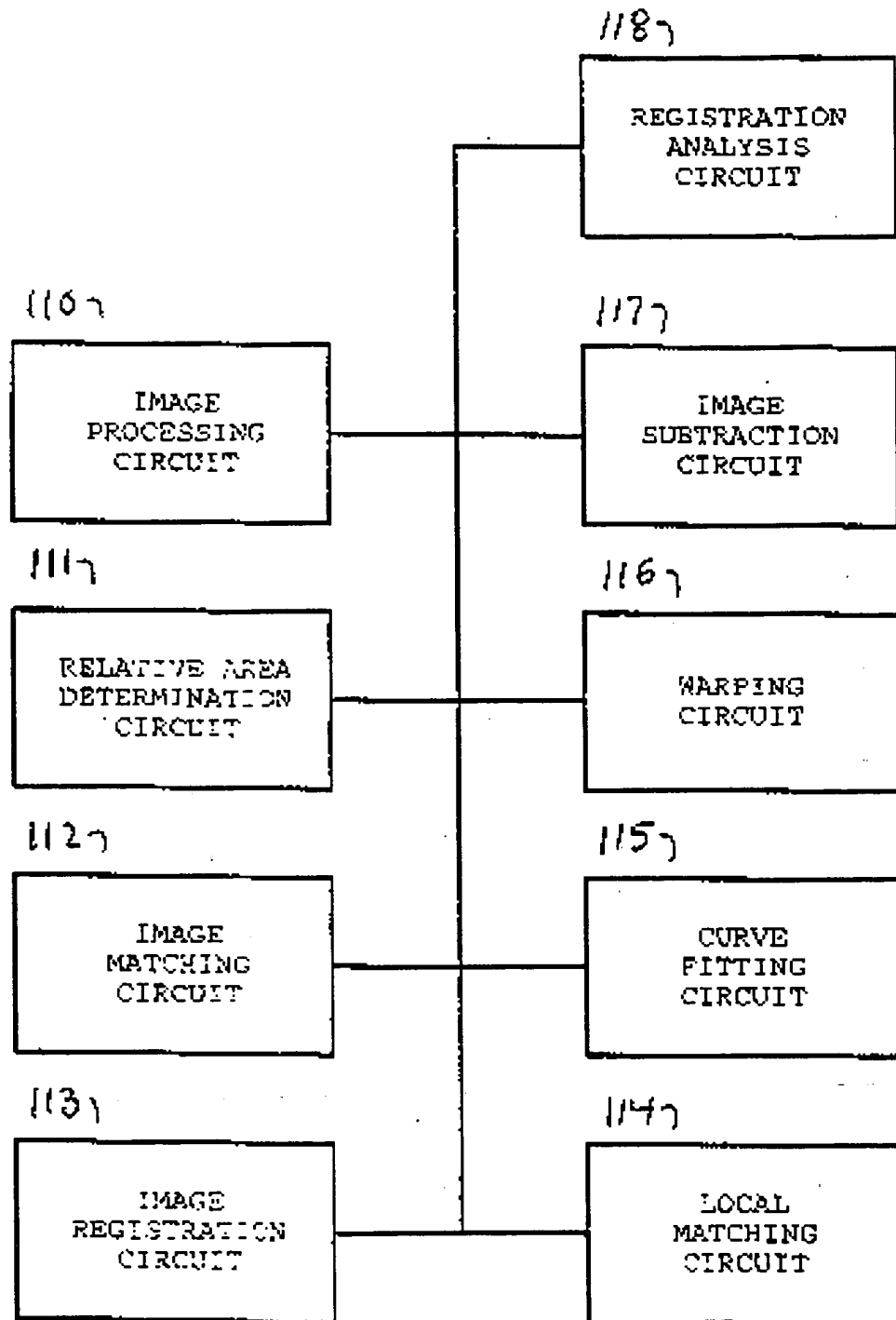


FIG. 14

THIS PAGE BLANK (USPTO)

THIS PAGE BLANK (USPTO)

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ BLACK BORDERS
- ☐ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
- ☐ FADED TEXT OR DRAWING
- ☐ BLURRED OR ILLEGIBLE TEXT OR DRAWING
- ☐ SKEWED/SLANTED IMAGES
- ☒ COLOR OR BLACK AND WHITE PHOTOGRAPHS
- ☐ GRAY SCALE DOCUMENTS
- ☐ LINES OR MARKS ON ORIGINAL DOCUMENT
- ☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
- ☐ OTHER: _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.

THIS PAGE BLANK (USPTO)